

# Haemodynamics

**Dr. PRIYANKA SACHDEV , MD**

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Apoptosis & Necrosis*



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Inflammation*



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Haemodynamic Disorder*



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# OVERVIEW

- Oedema
- Hyperamia and congestion
- Thrombosis
- Embolism
- Ischemia
- Infaction
- Schock



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# OEDEMA

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# OVERVIEW

- Definition
- Normal tissue exchange
- Pathogenesis
- Types of oedema fluid
- Important types of oedema

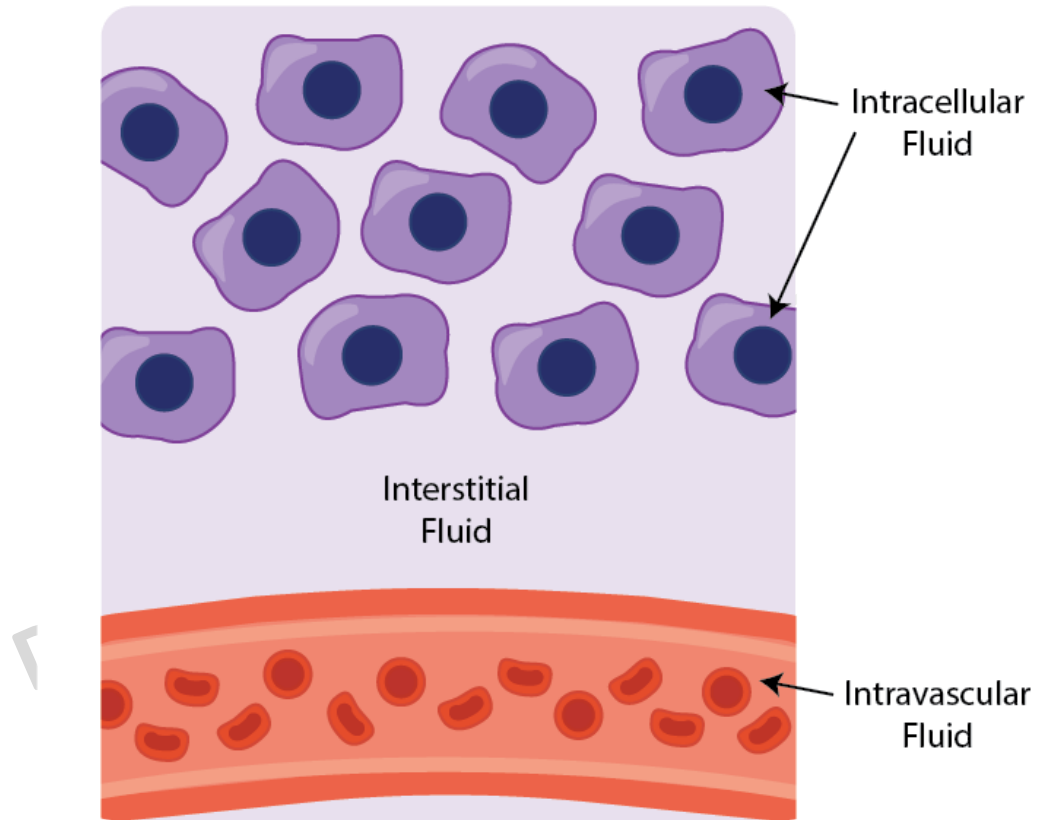


# Definition

- **Edema** is defined as abnormal and excessive accumulation of fluid in the interstitial tissue space
- **Effusions** is defined as abnormal and excessive accumulation of fluid in body cavities

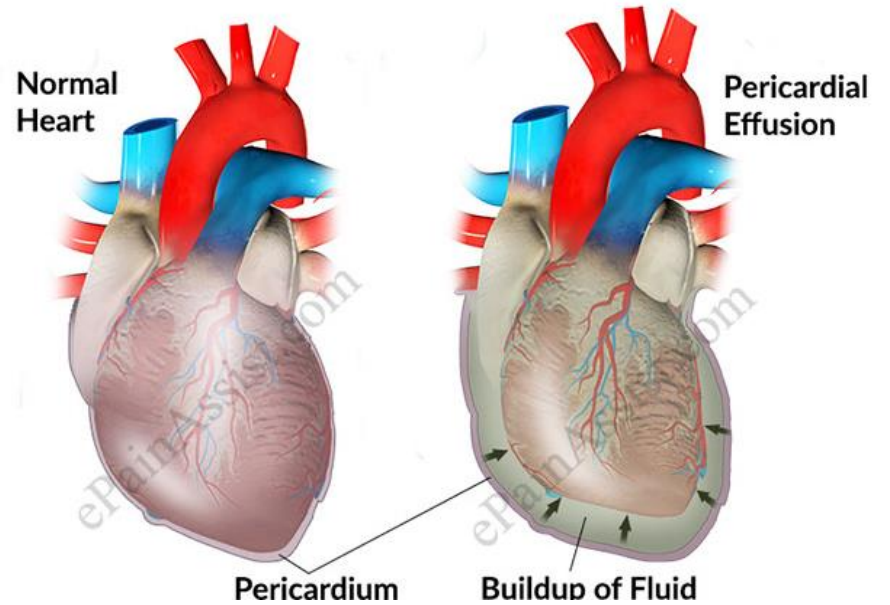
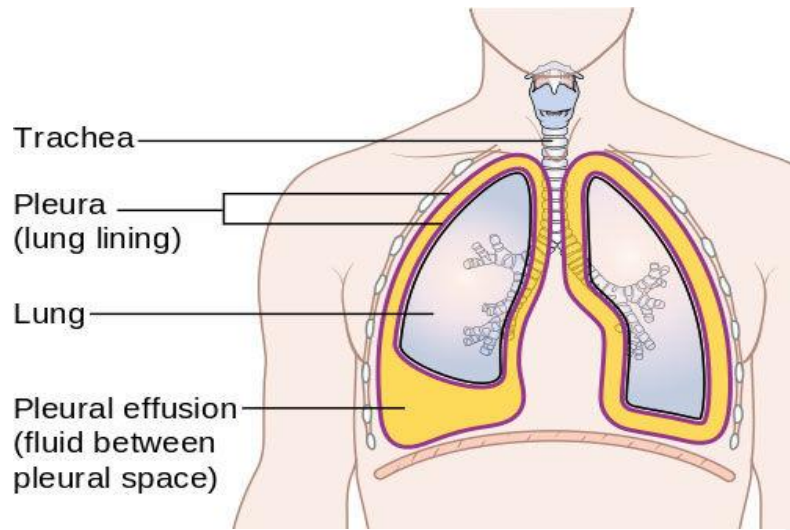


Dr. P



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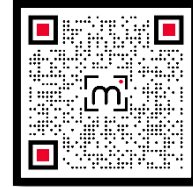
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- **Definition**
- **Normal tissue exchange**
- **Pathogenesis**
- **Types of oedema fluid**
- **Important types of oedema**

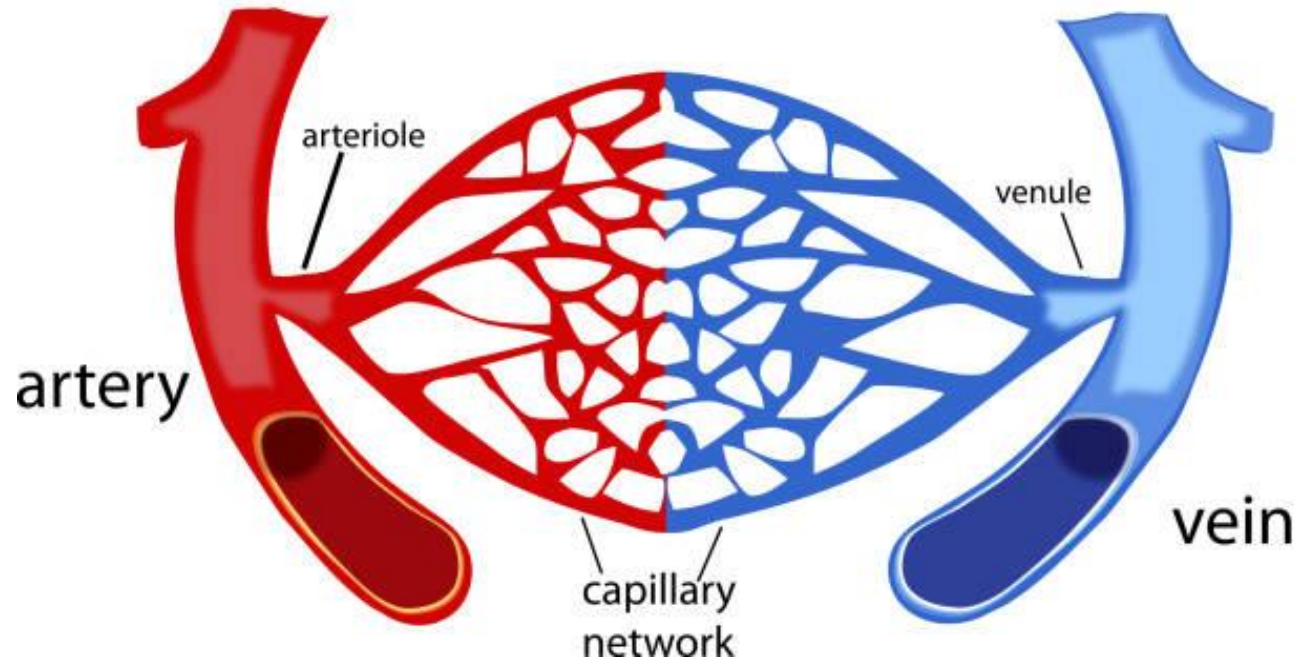
# Normal fluid exchange

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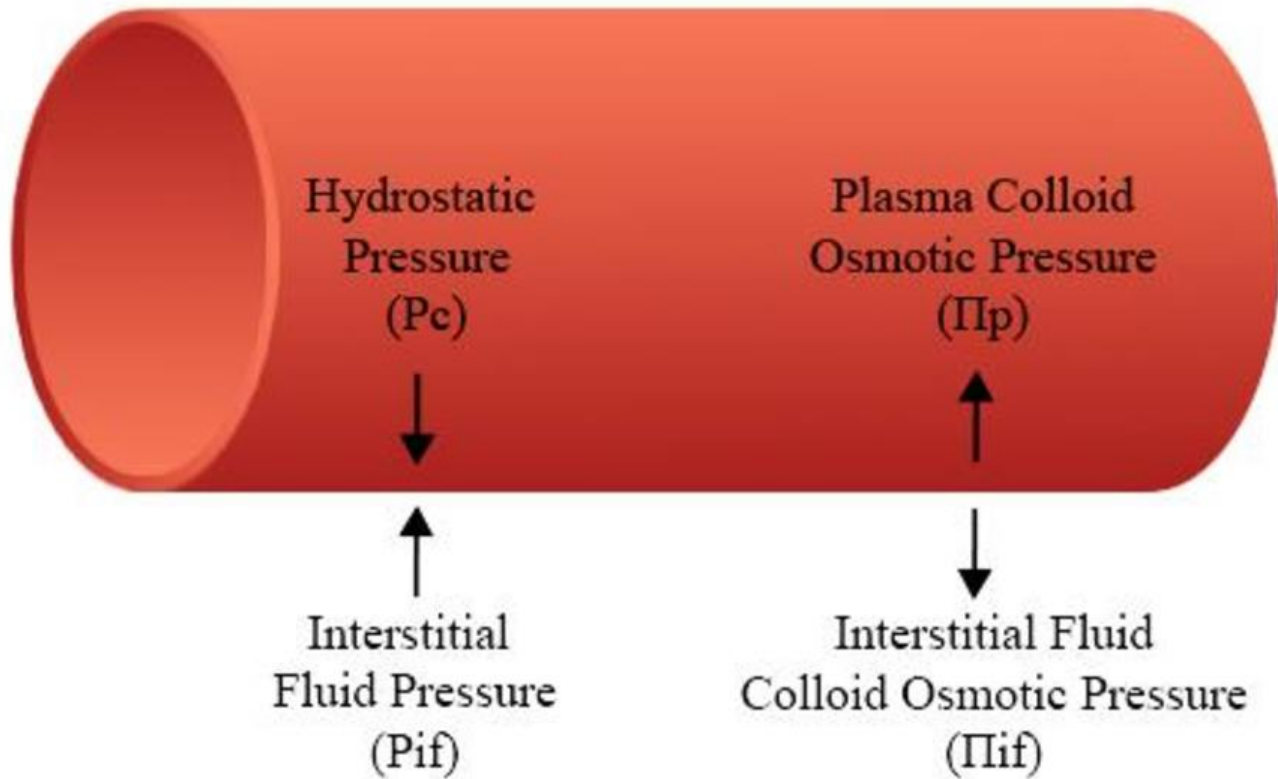
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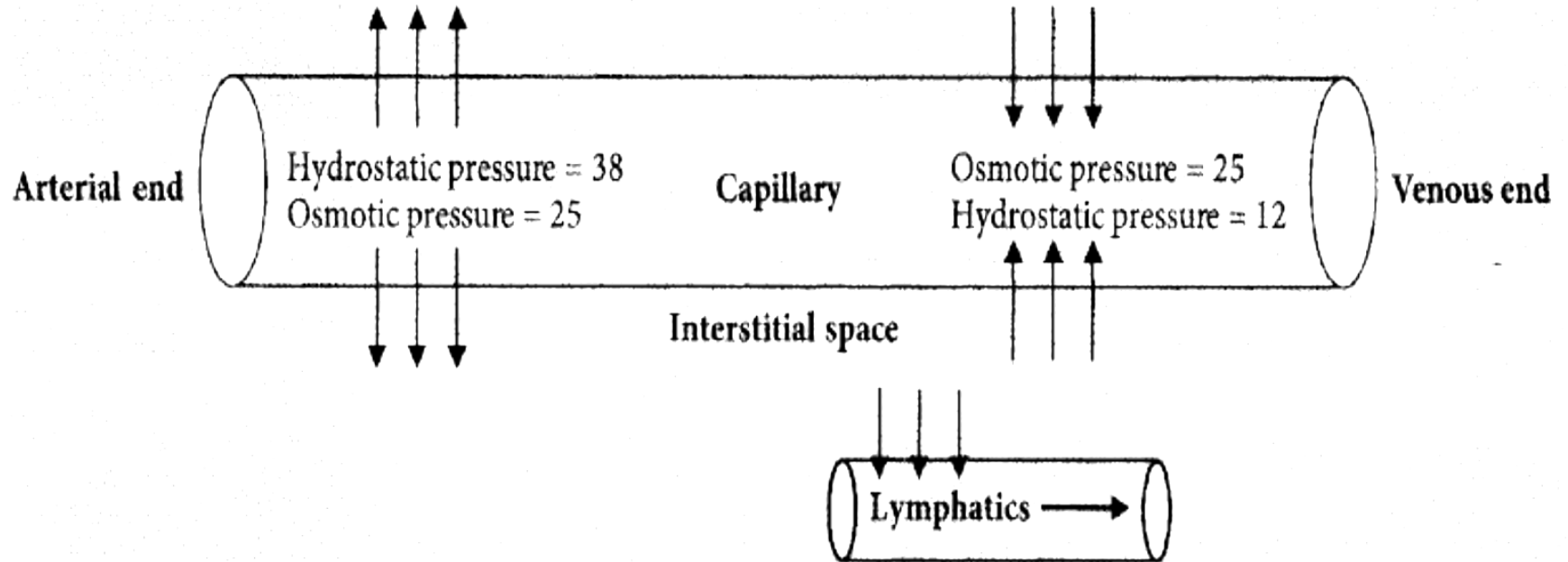


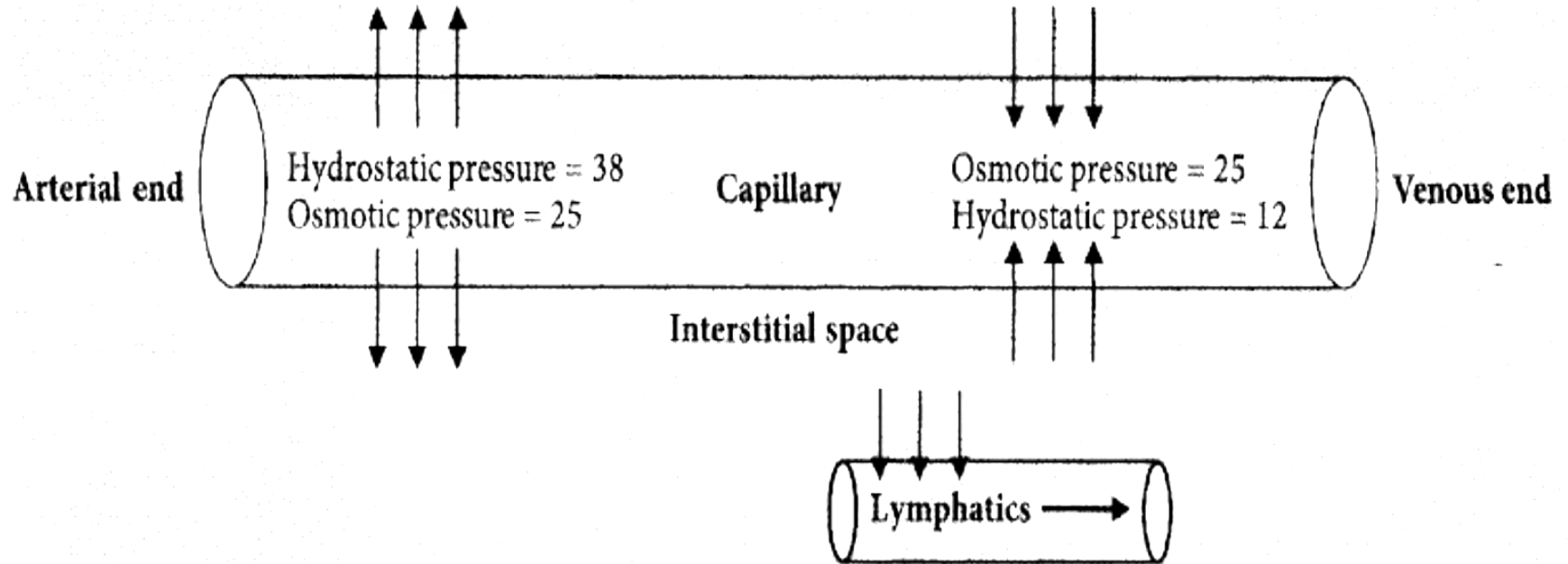
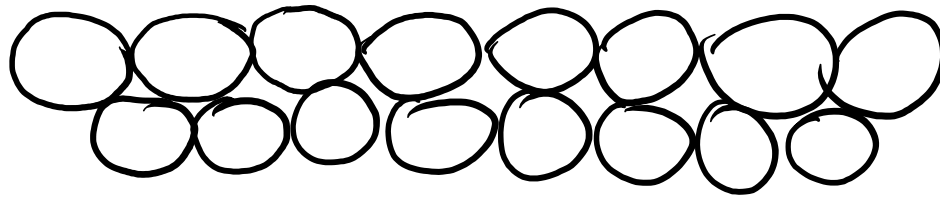
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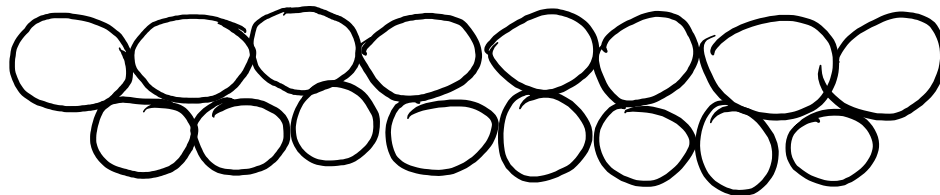








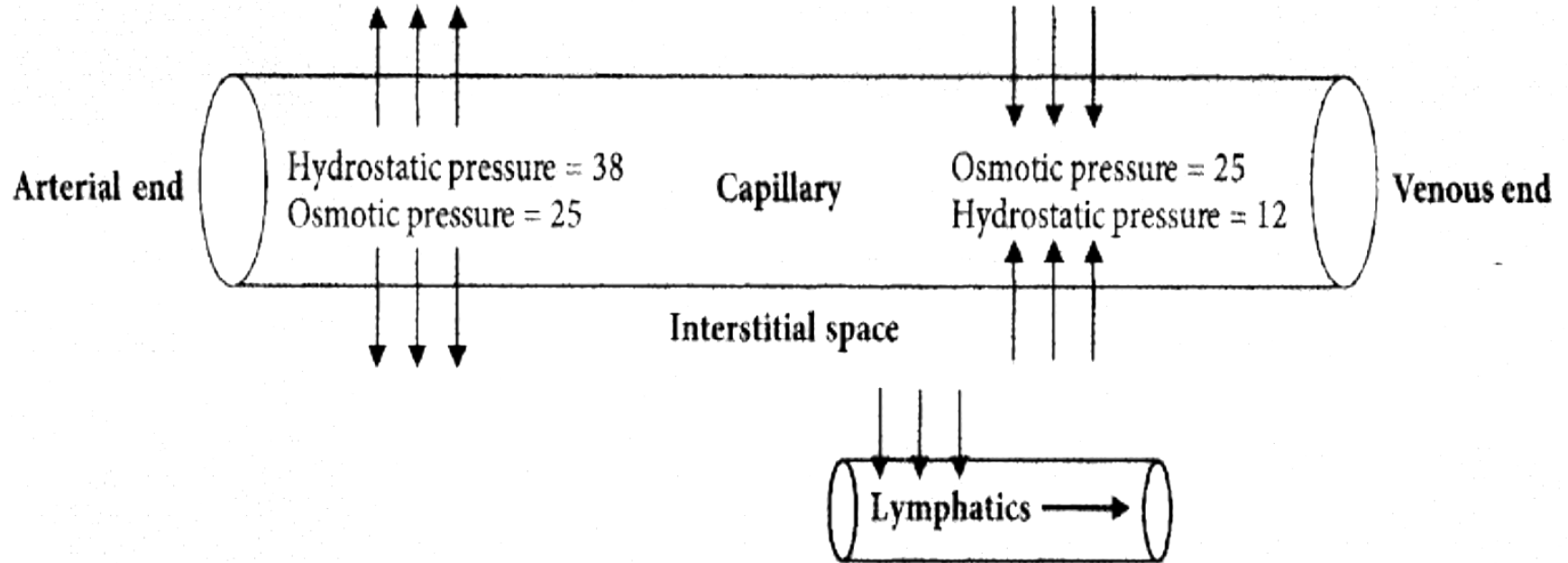


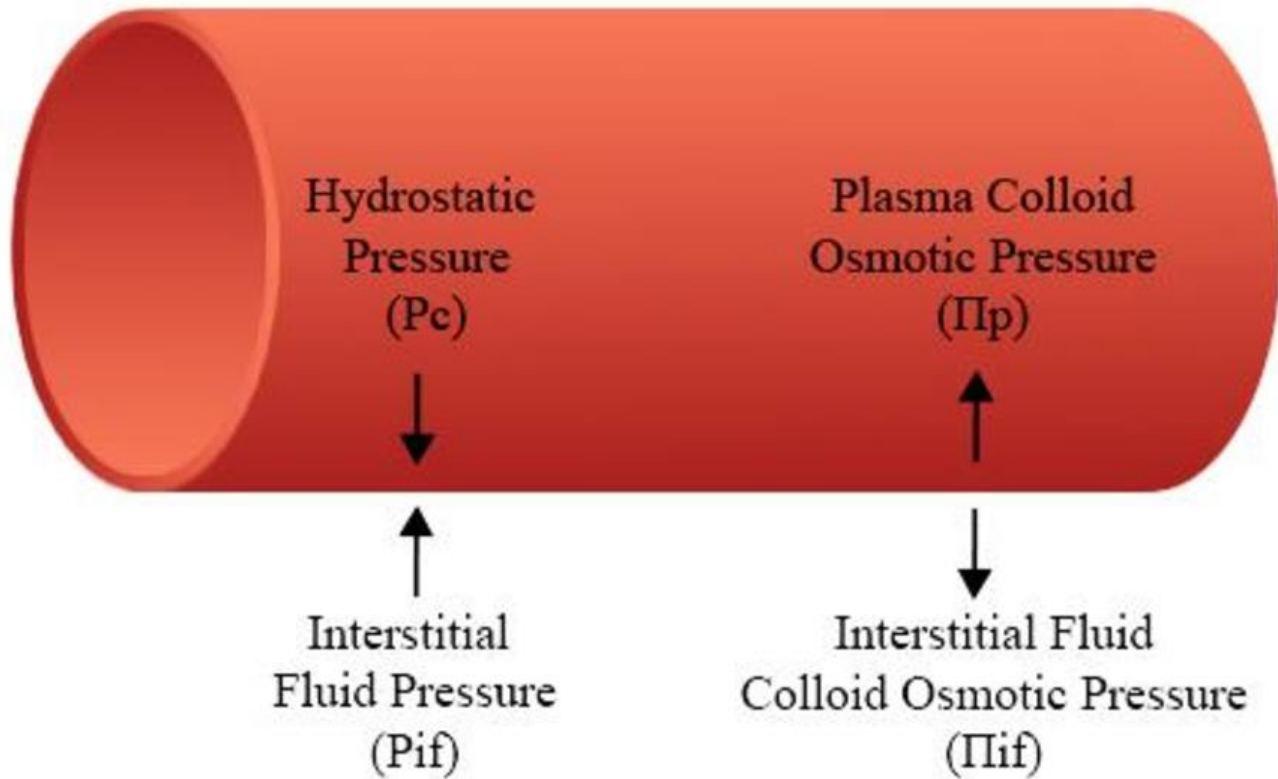


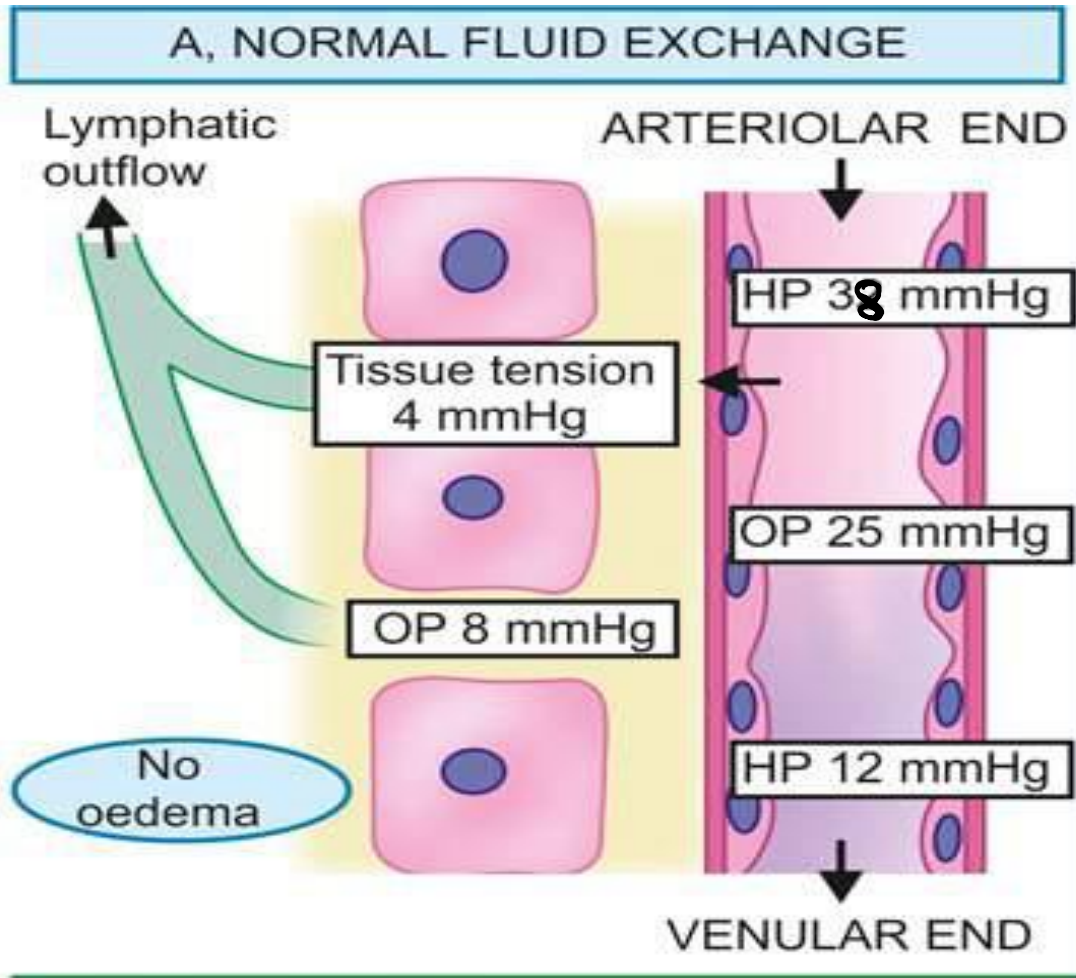
I.  $HP = 4$



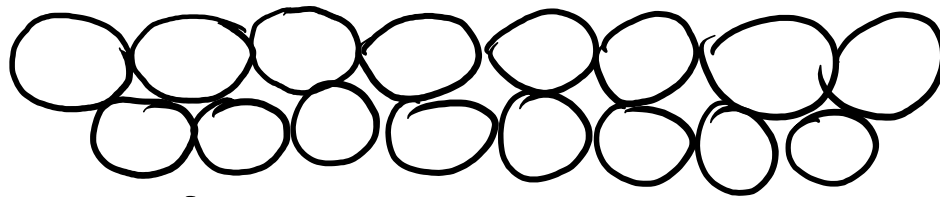
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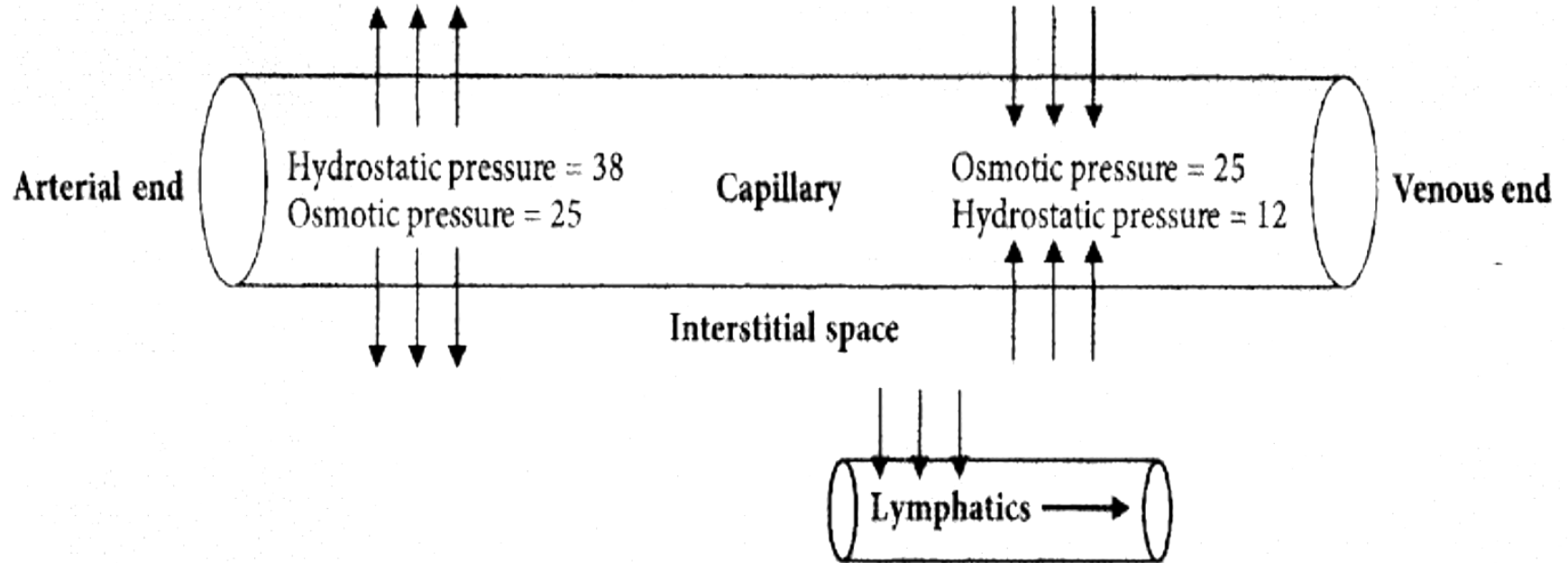
- **Hydrostatic pressure in the capillaries**, i.e., capillary blood pressure creates an **outward driving force** i.e. push water and salts out of capillaries into the interstitial space
- **Osmotic pressure in the capillaries** creates an **inward driving force**, ie. pull water and salts into vessels
- **Hydrostatic pressure of interstitial space (minor)** creates an **inward driving force**, ie. push water and salts into vessels
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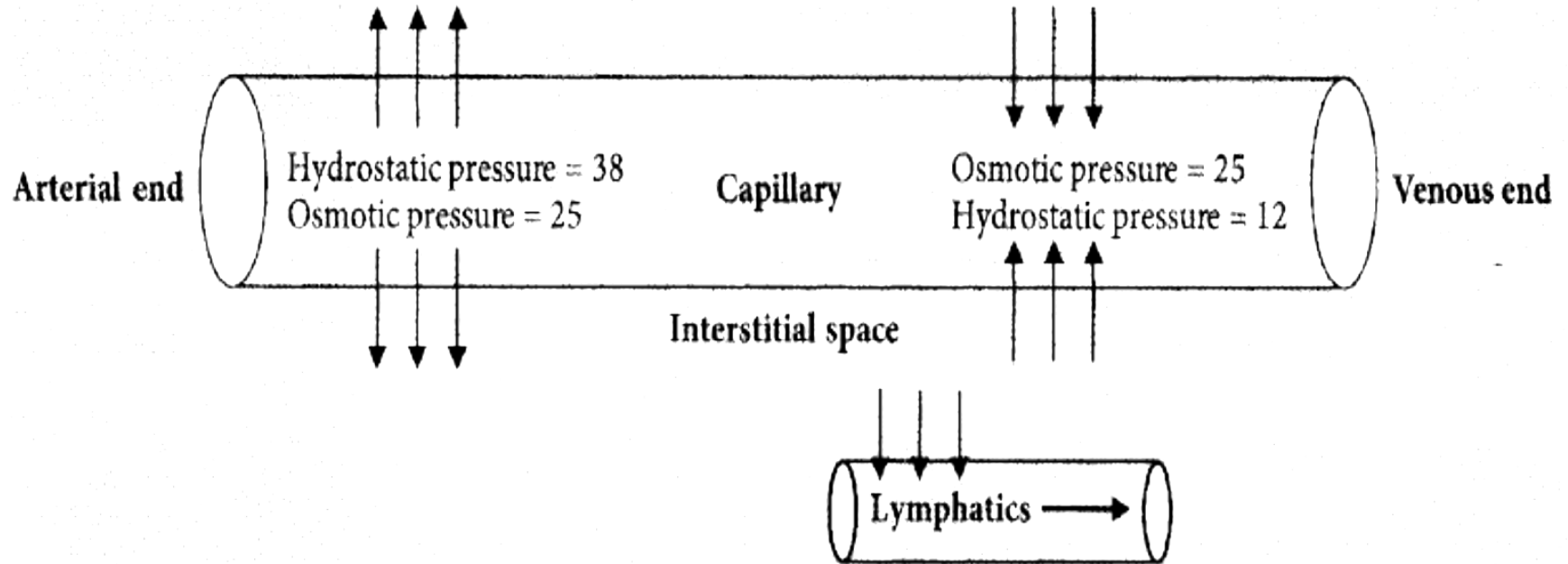
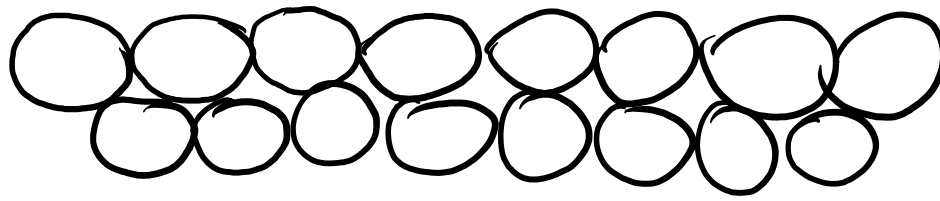
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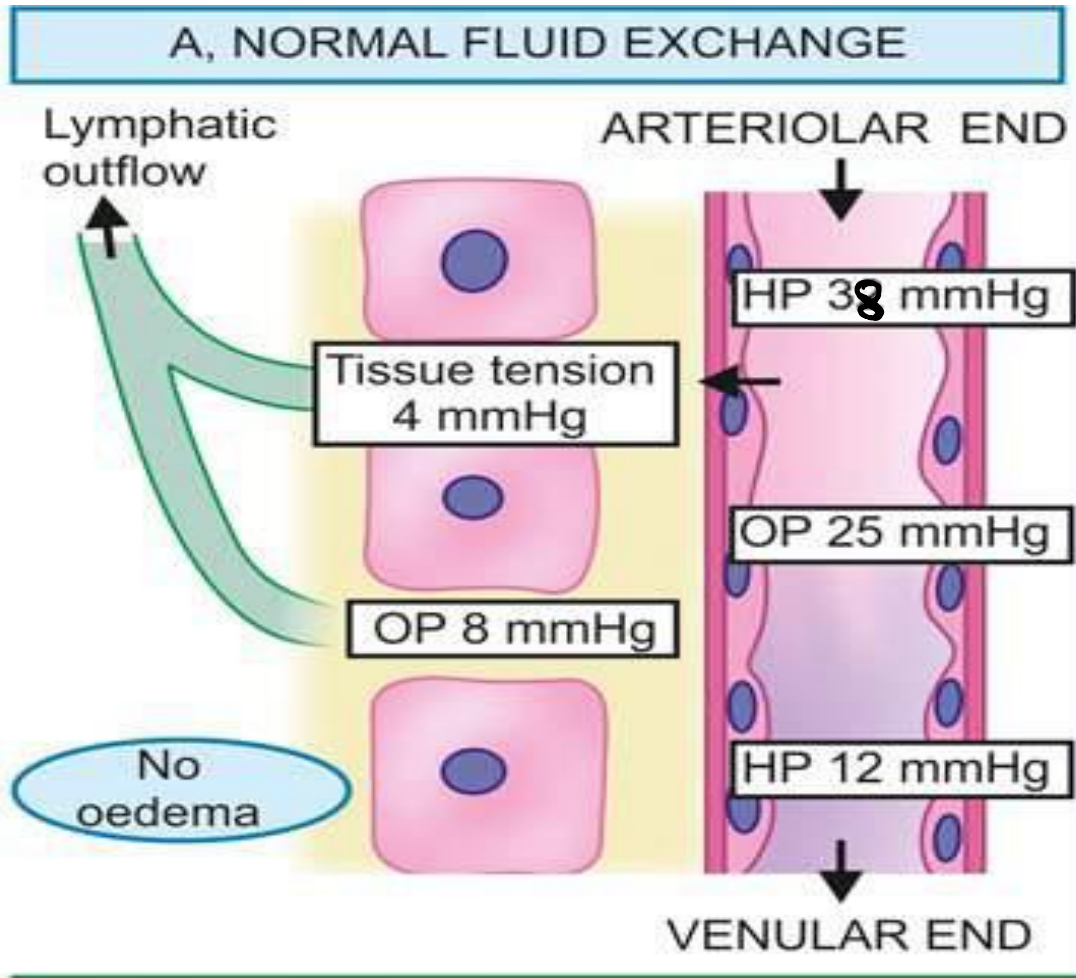


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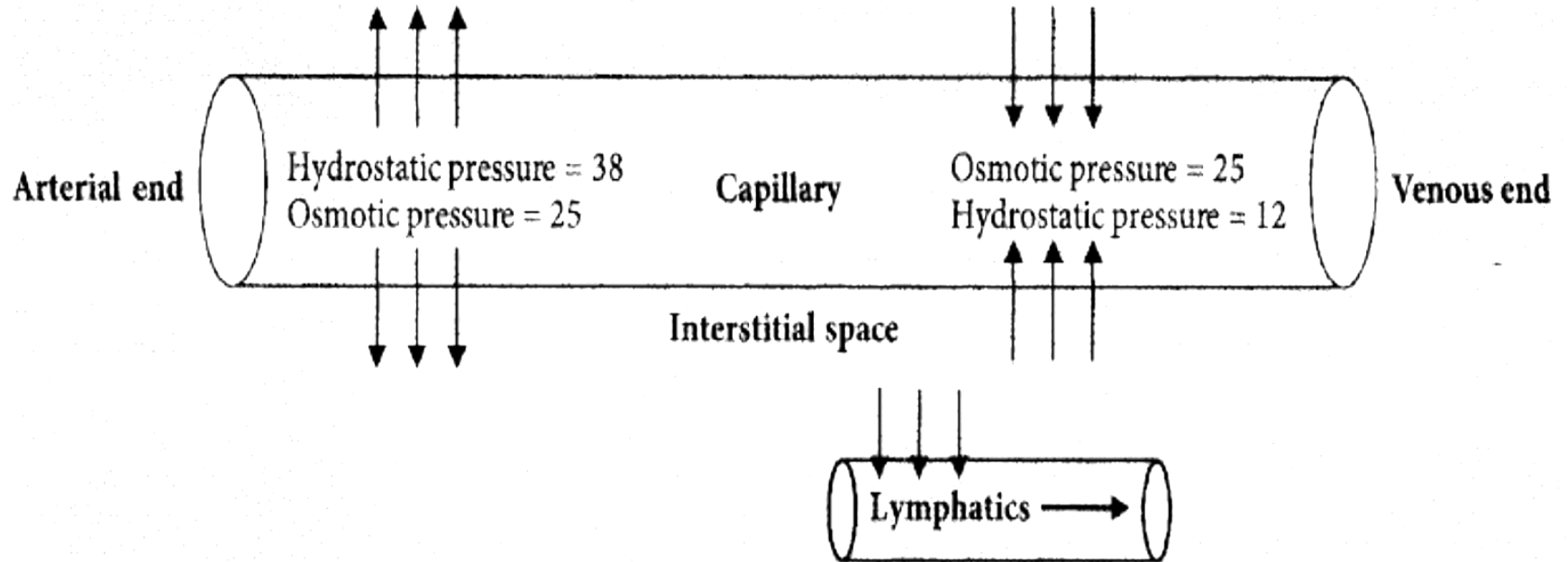








- At the arterial (proximal) end of capillary the hydrostatic pressure is **38 mmHg**
- At the venous end (distal) end of capillary the hydrostatic pressure is **12 mmHg.**
- Capillary osmotic pressure throughout is **25 mmHg**

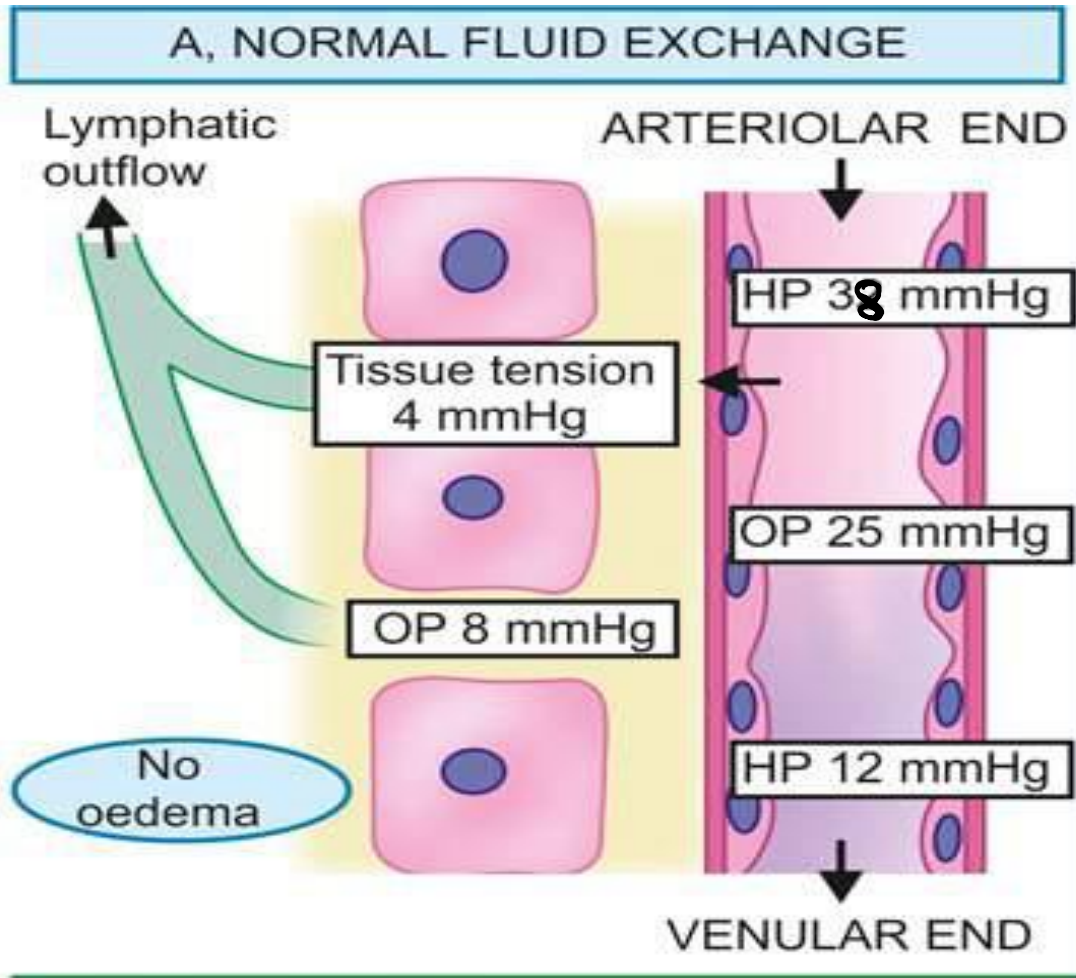


## At arterial end →

- Hydrostatic pressure (outward force) > osmotic pressure (inward force)
- Net Outward driving force at arterial end of capillary =  $38 - 25 = 13$  mmHg
- Fluid comes out from capillary into the interstitial space.

## At venous end →

- Osmotic pressure (inward pressure) > hydrostatic pressure (outward pressure)
- Net Inward-driving force at venous end of capillary =  $25 - 12 = 13$  mmHg.
- Fluid comes back in the capillary from interstitial space.



- Any excessive interstitial fluid is removed by **lymphatics** and ultimately returns to the bloodstream via thoracic ducts.
- So, **normally there is no edema** because at arterial end fluid comes out from the capillary, but returns back to the capillary at venous end

Under normal circumstances



**The tendency of capillary hydrostatic pressure to push water and salts out of capillaries into the interstitial space is **balanced** by the tendency of plasma colloid osmotic pressure to pull water and salts back into vessels.**

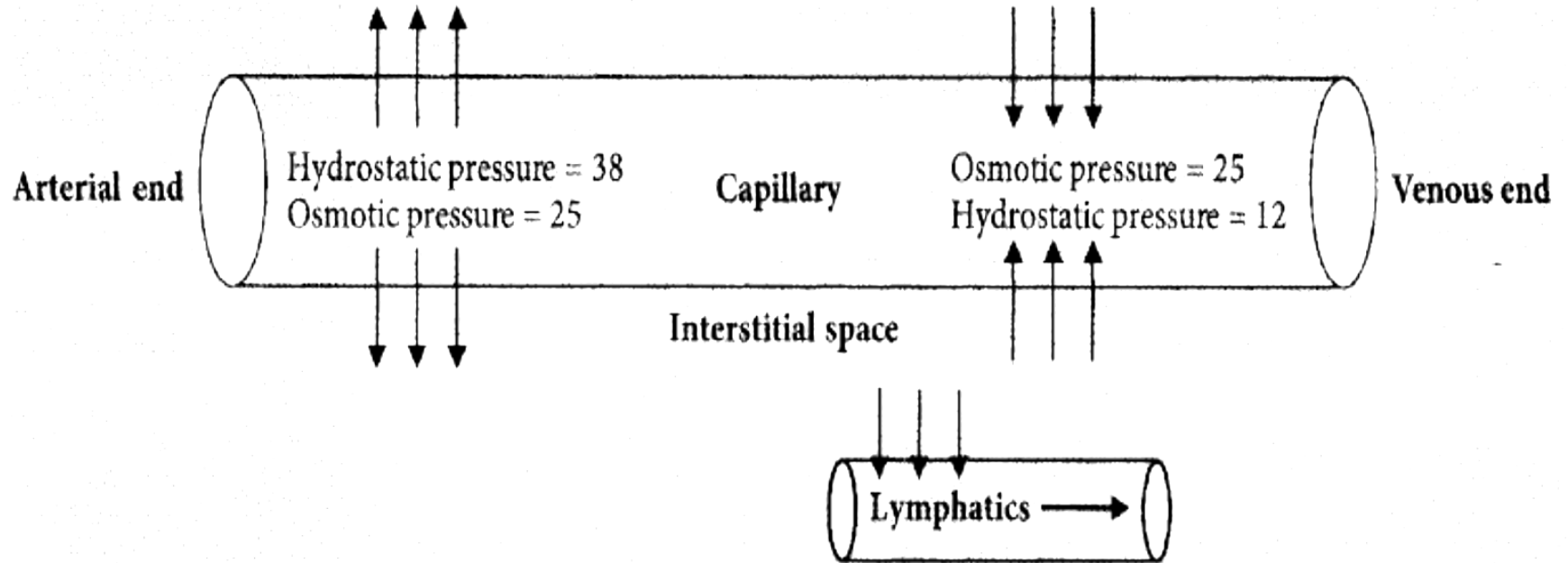


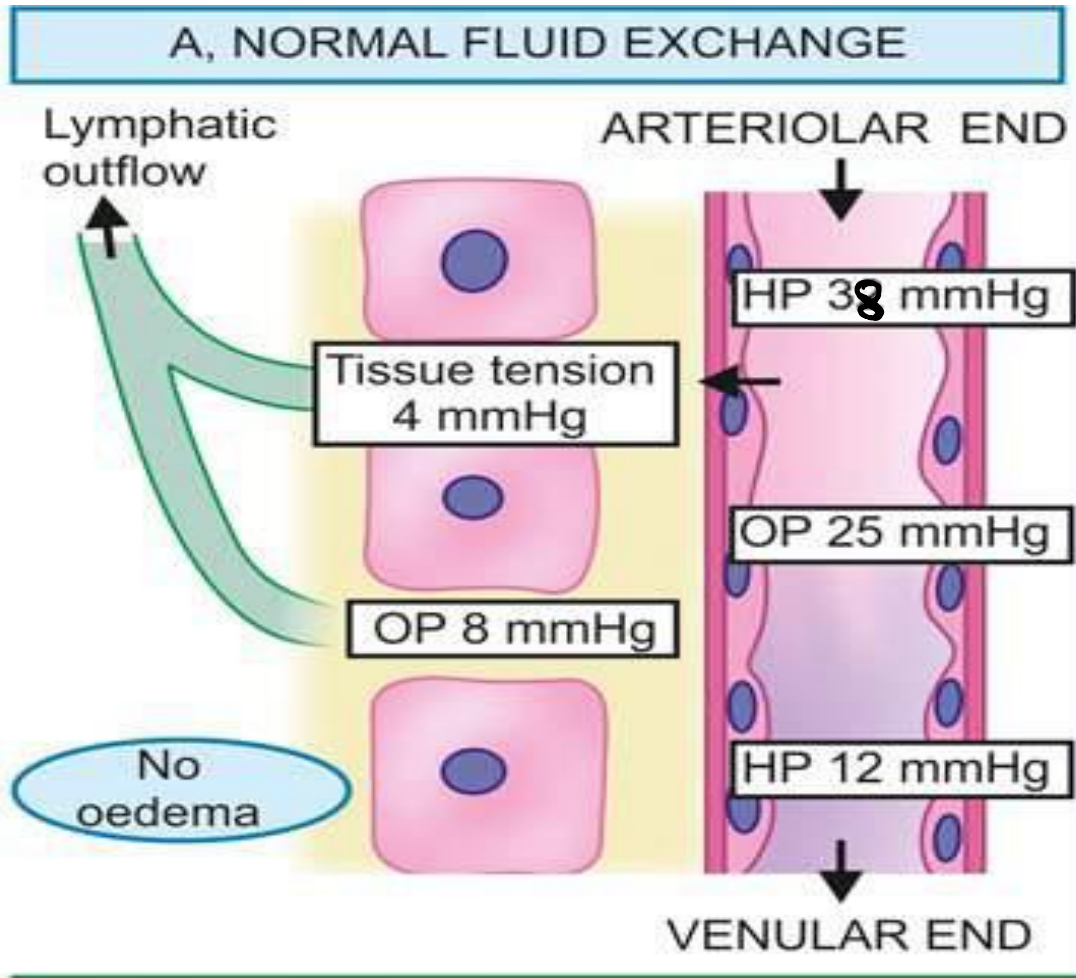
There is usually a small net movement of fluid into the interstitium, but this drains into lymphatic vessels and ultimately returns to the bloodstream via the thoracic duct,



So the tissues is **“dry” (no oedema)**

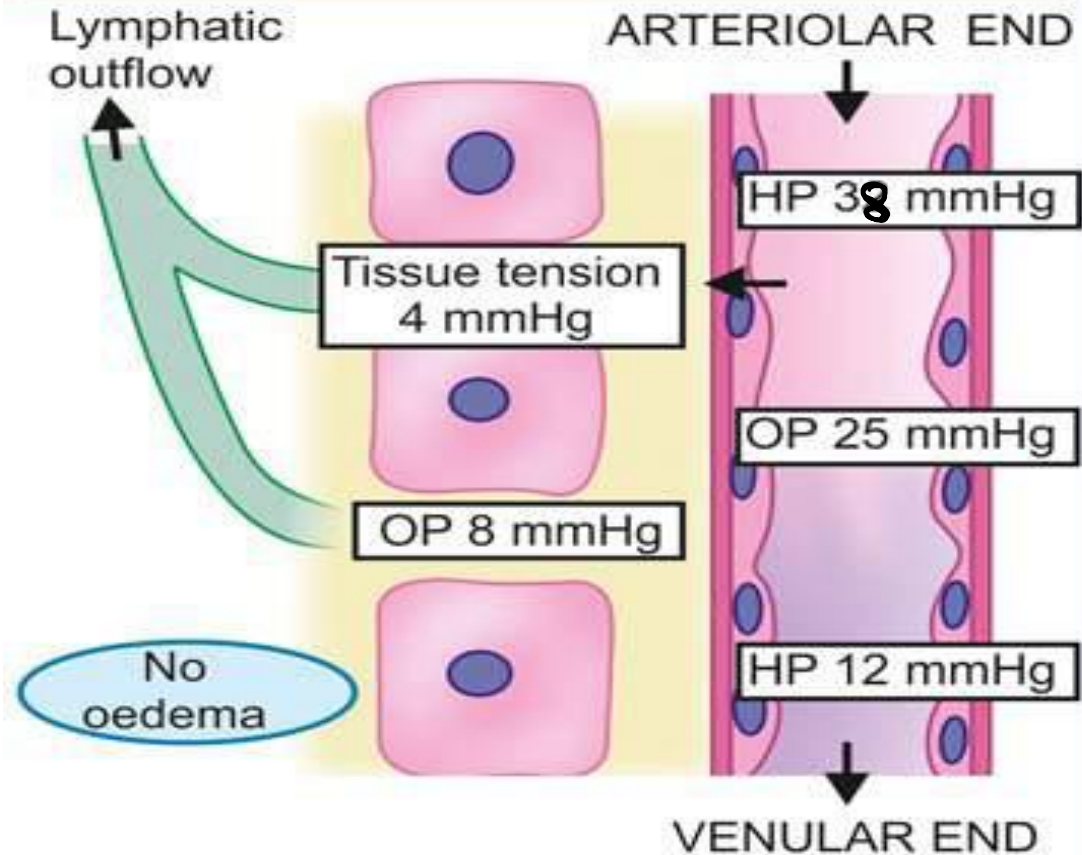






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## A, NORMAL FLUID EXCHANGE

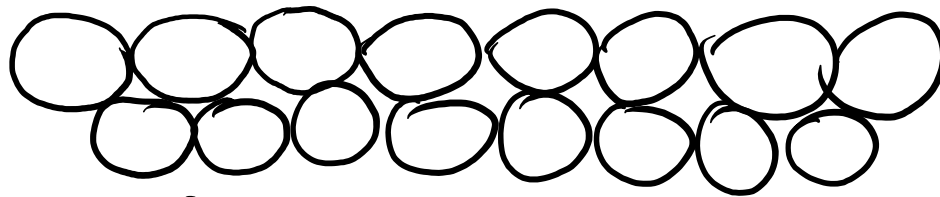


# **OVERVIEW**

- **Definition**
- **Normal tissue exchange**
- **Pathogenesis**
- **Types of oedema fluid**
- **Important types of oedema**

# **Pathogenesis of edema**

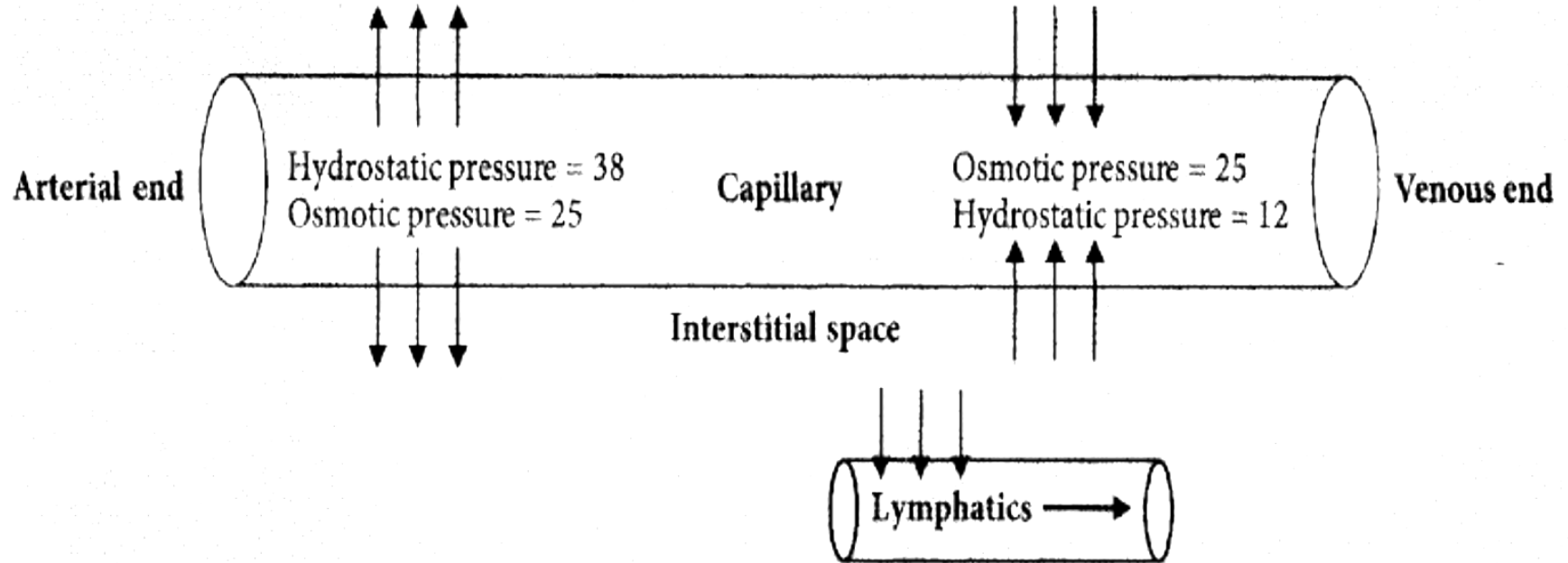
- **1. Increased capillary hydrostatic pressure**
- **2. Decreased plasma oncotic pressure**
- **3. Lymphatic obstruction**
- **4. Tissue factors (increased oncotic pressure and decreased hydrostatic pressure of interstitial fluid)**
- **5. Sodium and water retention**
- **6. Increased capillary permeability (Inflammation)**

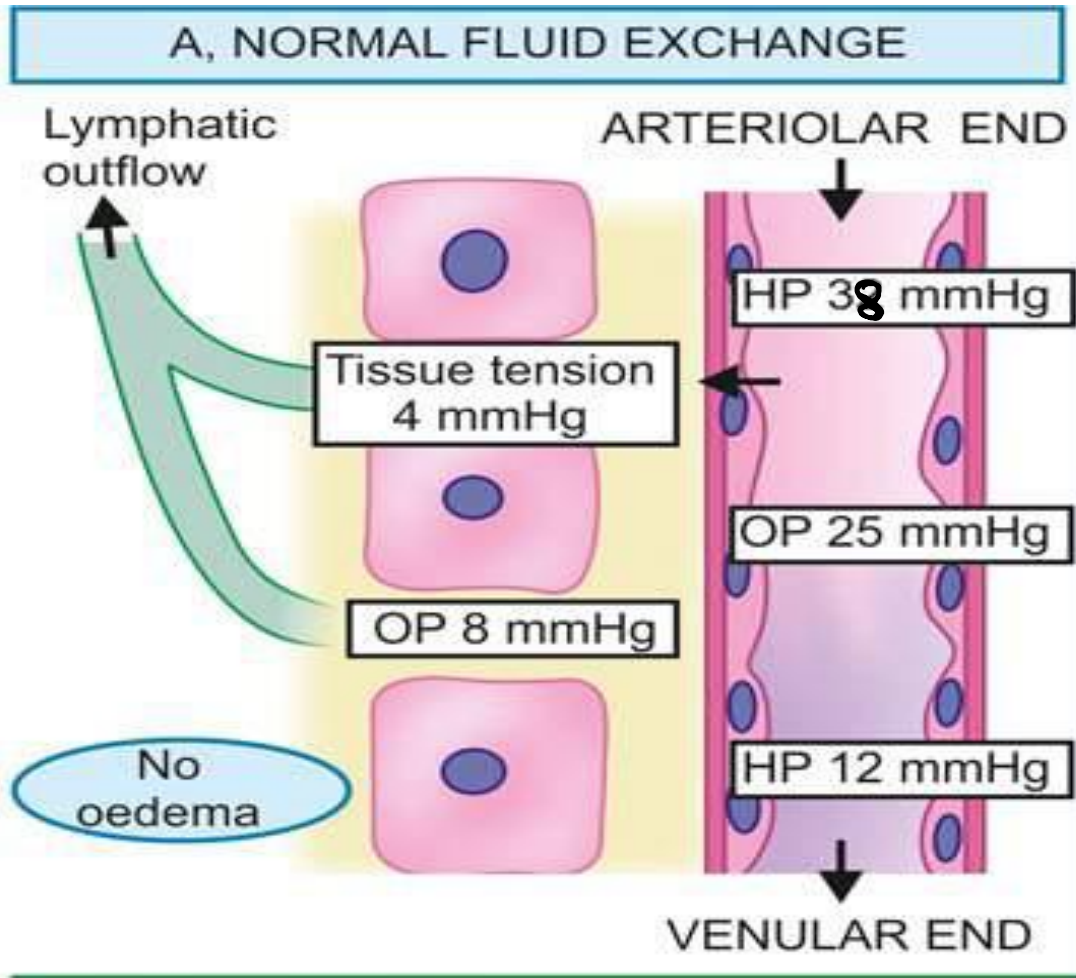


I.  $HP = 4$



I.  $OP = 8$







<b>Increased Hydrostatic Pressure</b>
<b>Impaired Venous Return</b>
Congestive heart failure Constrictive pericarditis Ascites (liver cirrhosis) Venous obstruction or compression Thrombosis External pressure (e.g., mass) Lower extremity inactivity with prolonged dependency
<b>Arteriolar Dilation</b>
Heat Neurohumoral dysregulation
<b>Reduced Plasma Osmotic Pressure (Hypoproteinemia)</b>
Protein-losing glomerulopathies (nephrotic syndrome) Liver cirrhosis (ascites) Malnutrition Protein-losing gastroenteropathy
<b>Lymphatic Obstruction</b>
Inflammatory Neoplastic Postsurgical Postirradiation
<b>Sodium Retention</b>
Excessive salt intake with renal insufficiency Increased tubular reabsorption of sodium Renal hypoperfusion Increased renin-angiotensin-aldosterone secretion
<b>Inflammation</b>
Acute inflammation Chronic inflammation Angiogenesis

# 1. INCREASED CAPILLARY HYDROSTATIC PRESSURE

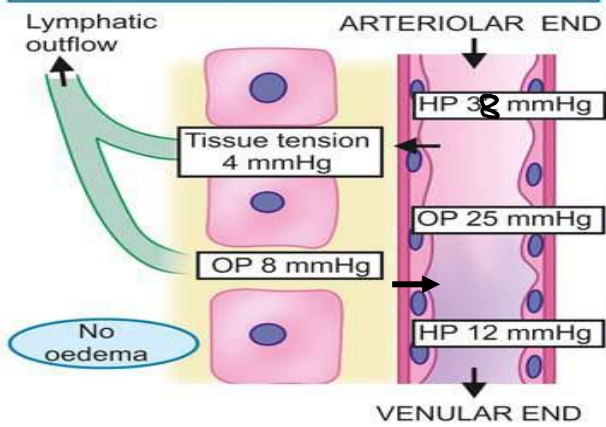
A rise in the hydrostatic pressure at the venular end of the capillary

↓  
Hydrostatic pressure at venous end > oncotic pressure (outward > inward)

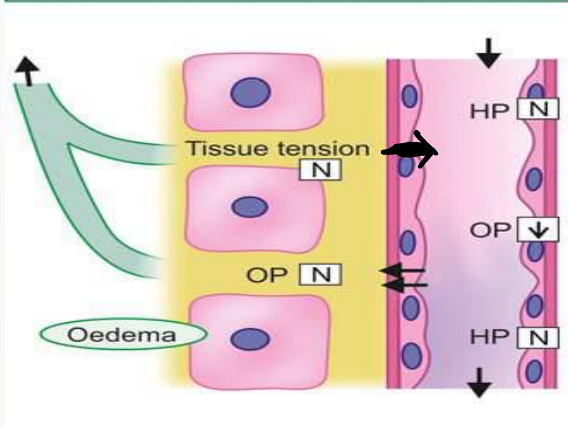
↓  
No reabsorption of fluid at the venular end

↓  
**Oedema**

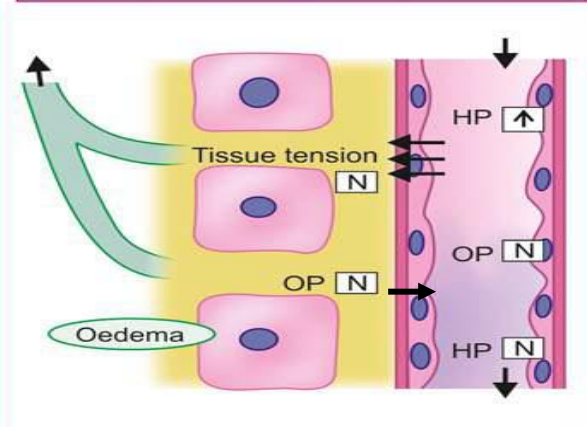
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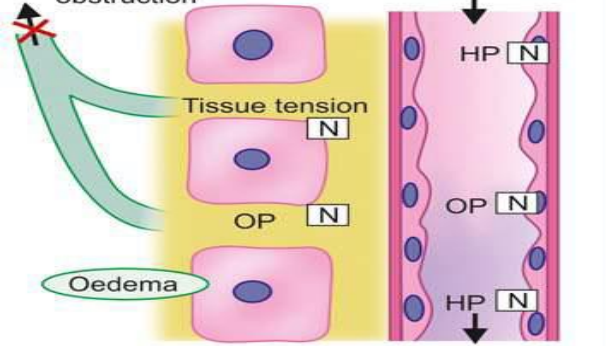
**B, ↓ PLASMA OSMOTIC PRESSURE**



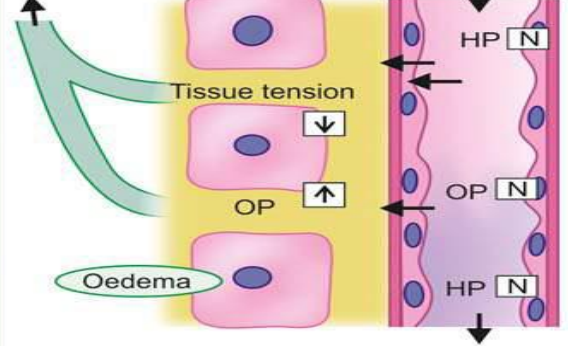
**C, ↑ CAPILLARY PRESSURE**



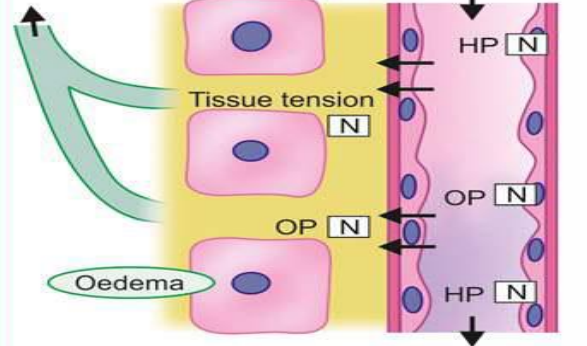
**D, Lymphoedema**



**E, TISSUE FACTORS**



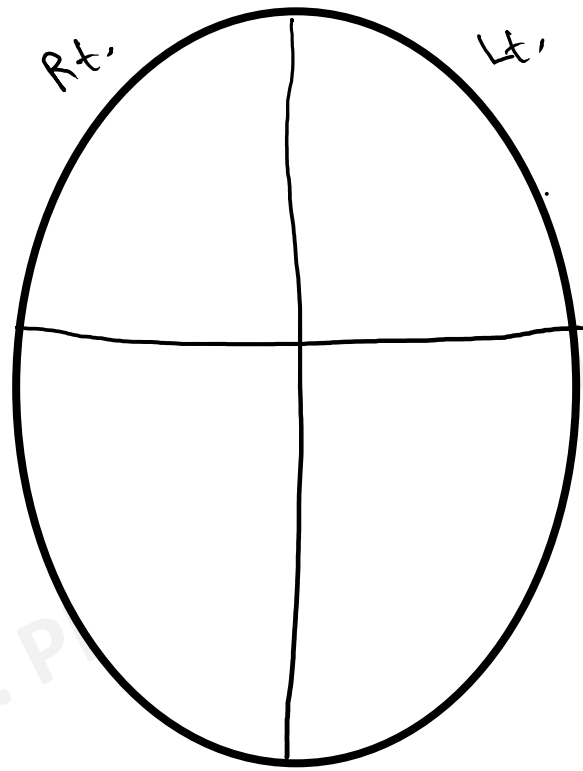
**F, ↑ CAPILLARY PERMEABILITY**



# Examples →

Increases in hydrostatic pressure are mainly caused by disorders that impair venous return

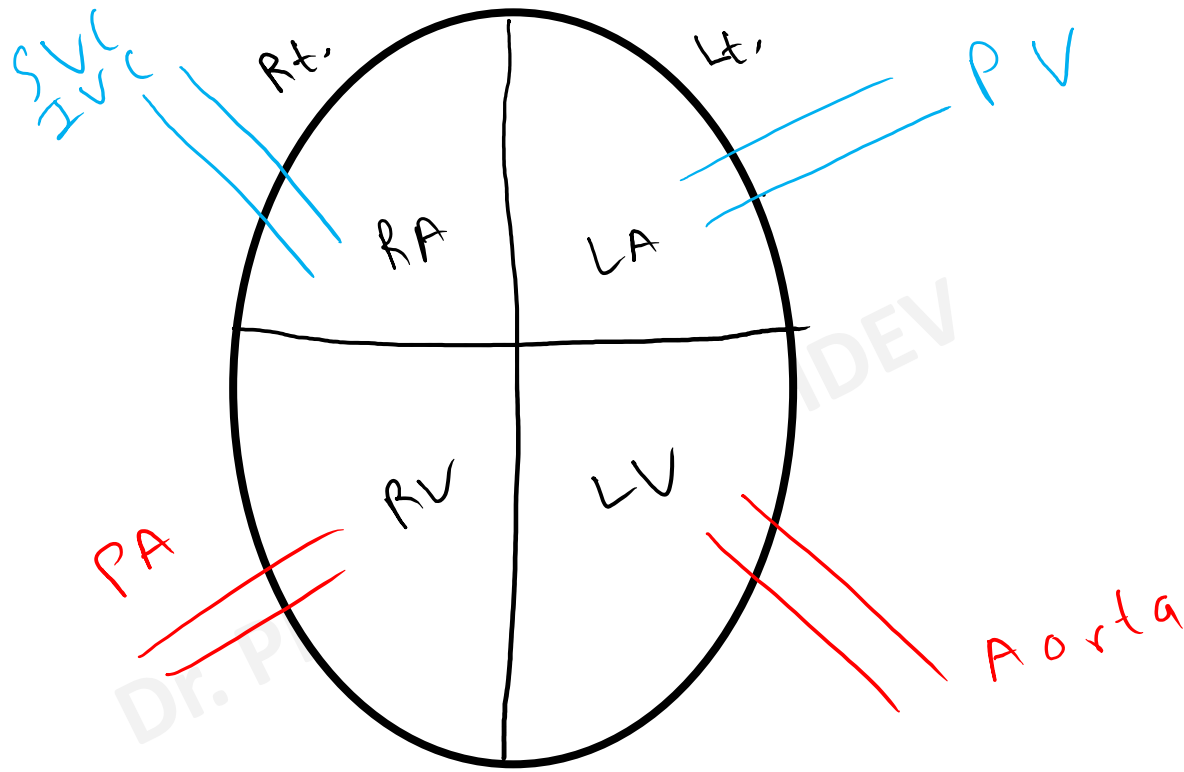
- **i) Oedema of cardiac disease** e.g. in congestive cardiac failure, constrictive pericarditis.
- **ii) Postural oedema** e.g. transient oedema of feet and ankles due to increased venous pressure seen in individuals Whose job involves standing for long hours such as traffic constables

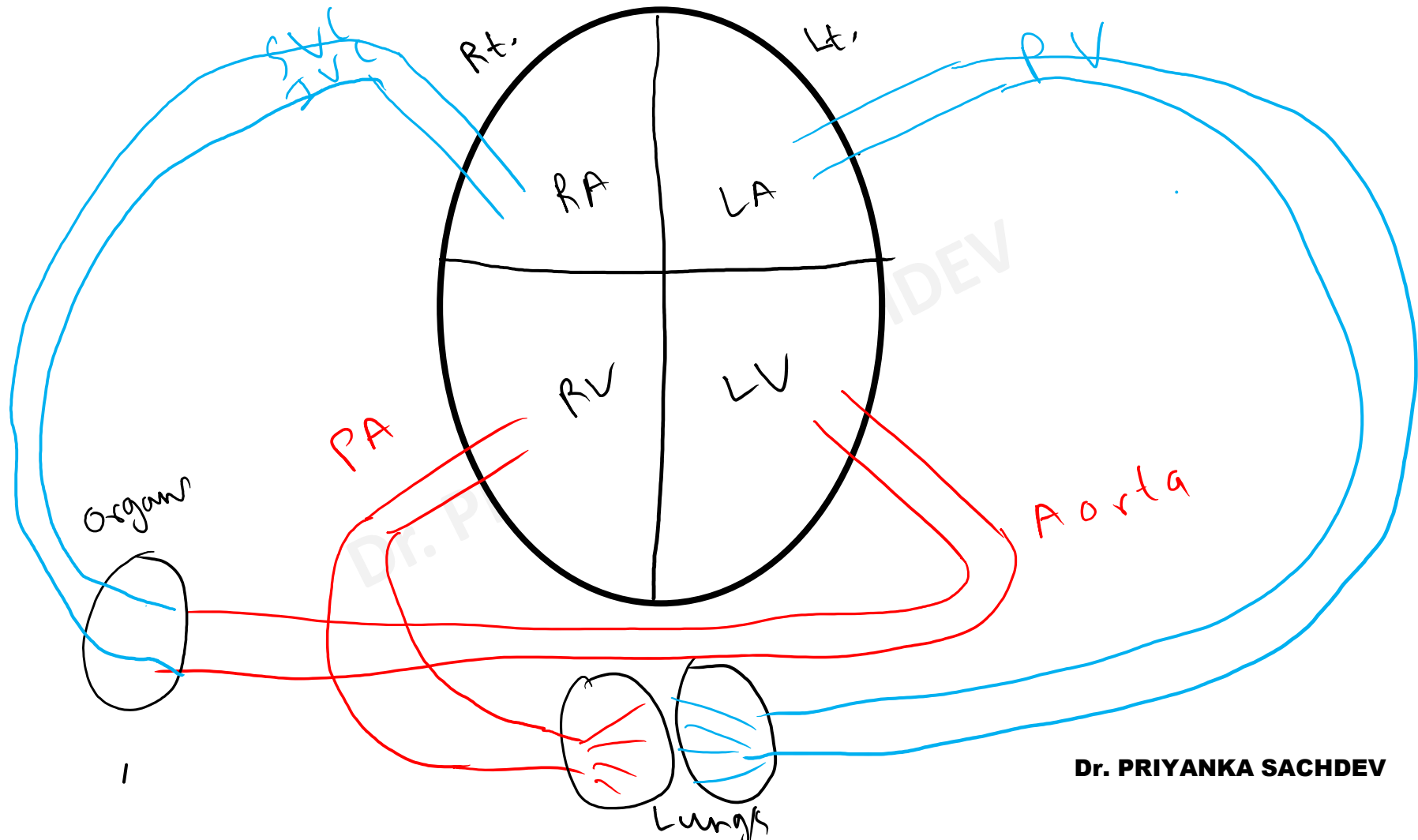


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# **Pathogenesis of edema**

- **1. Increased capillary hydrostatic pressure**
- **2. Decreased plasma oncotic pressure**
- **3. Lymphatic obstruction**
- **4. Tissue factors (increased oncotic pressure of interstitial fluid)**
- **5. Sodium and water retention**
- **6. Increased capillary permeability (Inflammation)**



## **2. DECREASED PLASMA ONCOTIC PRESSURE**

- The plasma oncotic pressure is exerted by the total amount of plasma proteins.
- **Albumin has four times higher plasma oncotic pressure than globulin;**
- **Thus it is hypoalbuminaemia that results in oedema.**

**A fall in the total plasma protein level (hypoproteinaemia of less than 5 g/dl)**



**Lowering of plasma oncotic pressure**

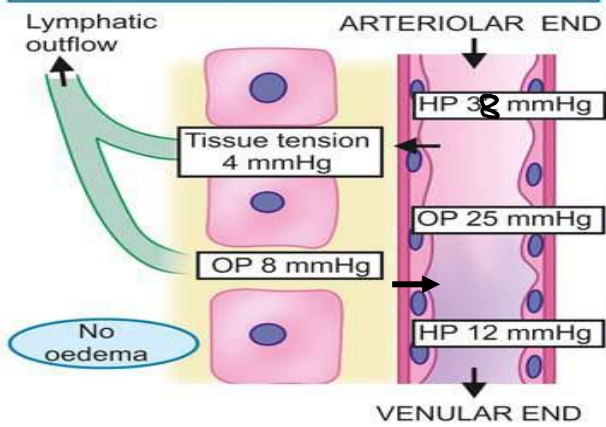


**Increased outward movement of fluid and decreased inward movement of fluid**

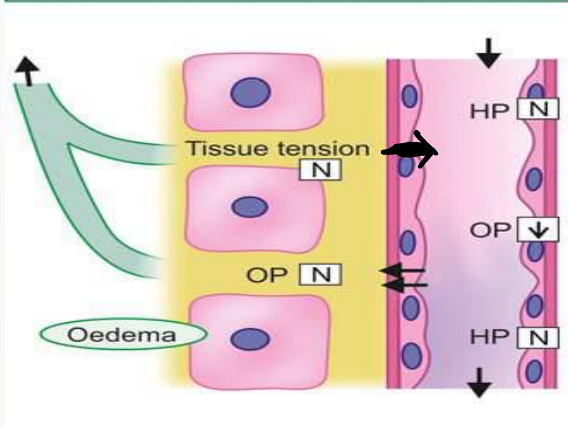


**Oedema**

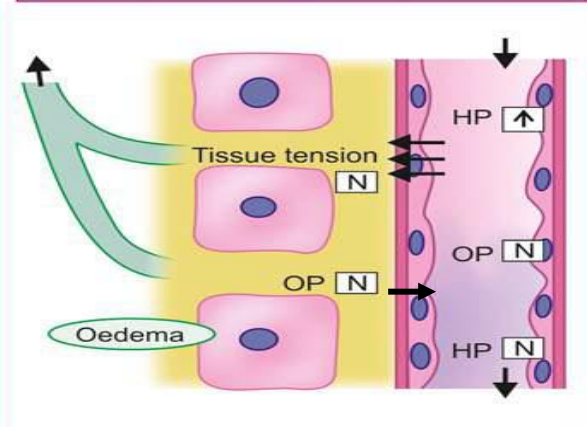
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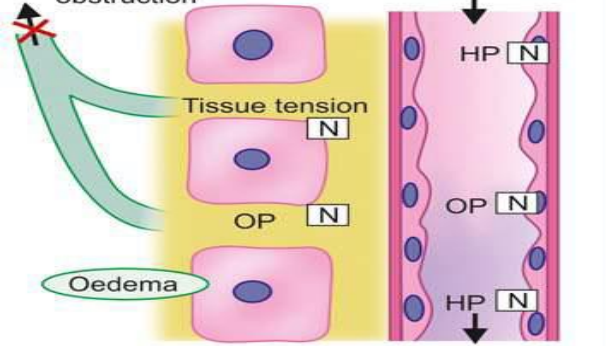
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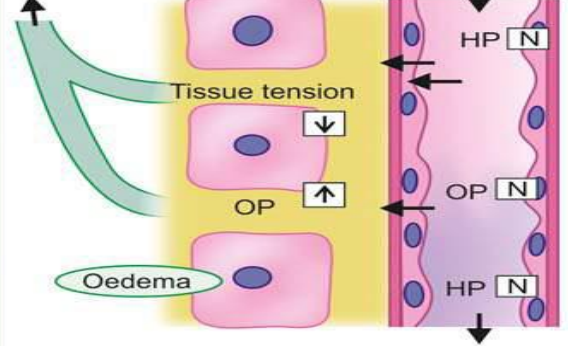
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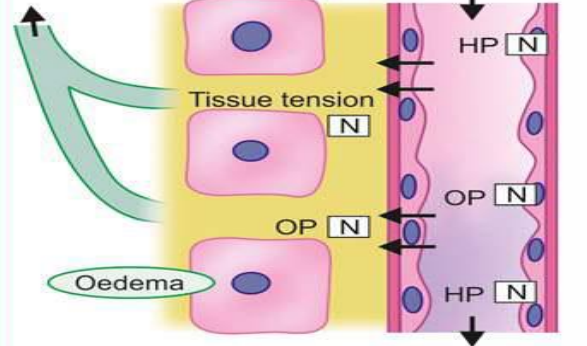
**D, Lymphoedema**



**E, TISSUE FACTORS**



**F, ↑ CAPILLARY PERMEABILITY**



**D, Lymphoedema**

**E, TISSUE FACTORS**

**F, ↑ CAPILLARY PERMEABILITY**

# REMEMBER→ edema takes place when

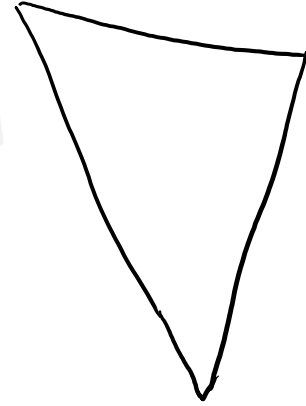
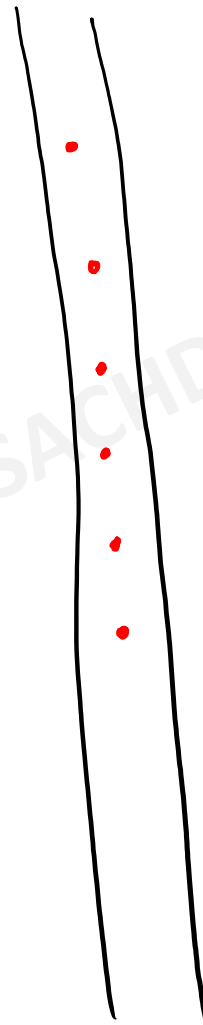
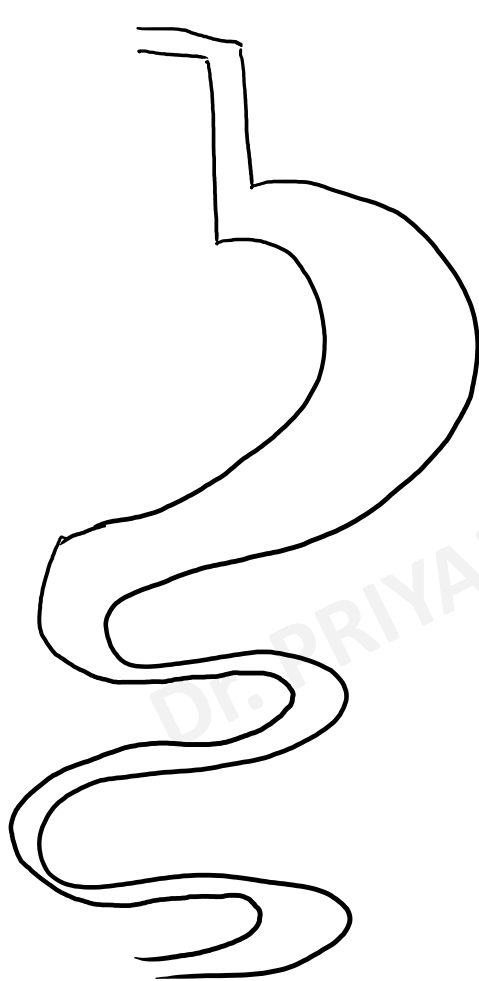
- Total plasma protein is **below 5 gm/dl** (normal 6-8 gm/dl)  
 $(5/8 \times 100) \cong 63\%$ .
- Albumin is **below 2.5 gm/dl** (normal 3.5-5gm/dl)

# Examples →

1. Inadequate synthesis of albumin → **severe liver diseases (end-stage cirrhosis)**

2. **Protein malnutrition**

3. Increased loss of albumin → **Nephrotic syndrome** in which albumin leaks into the urine through abnormally permeable glomerular capillaries.



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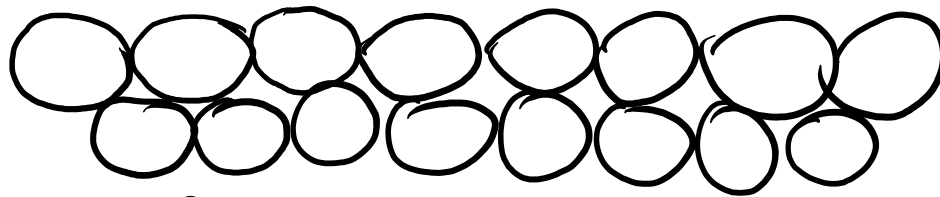
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### 3. LYMPHATIC OBSTRUCTION

- Normally, the interstitial fluid in the tissue spaces escapes by way of lymphatics.
- Obstruction to outflow of these channels → oedema, known as **lymphoedema**

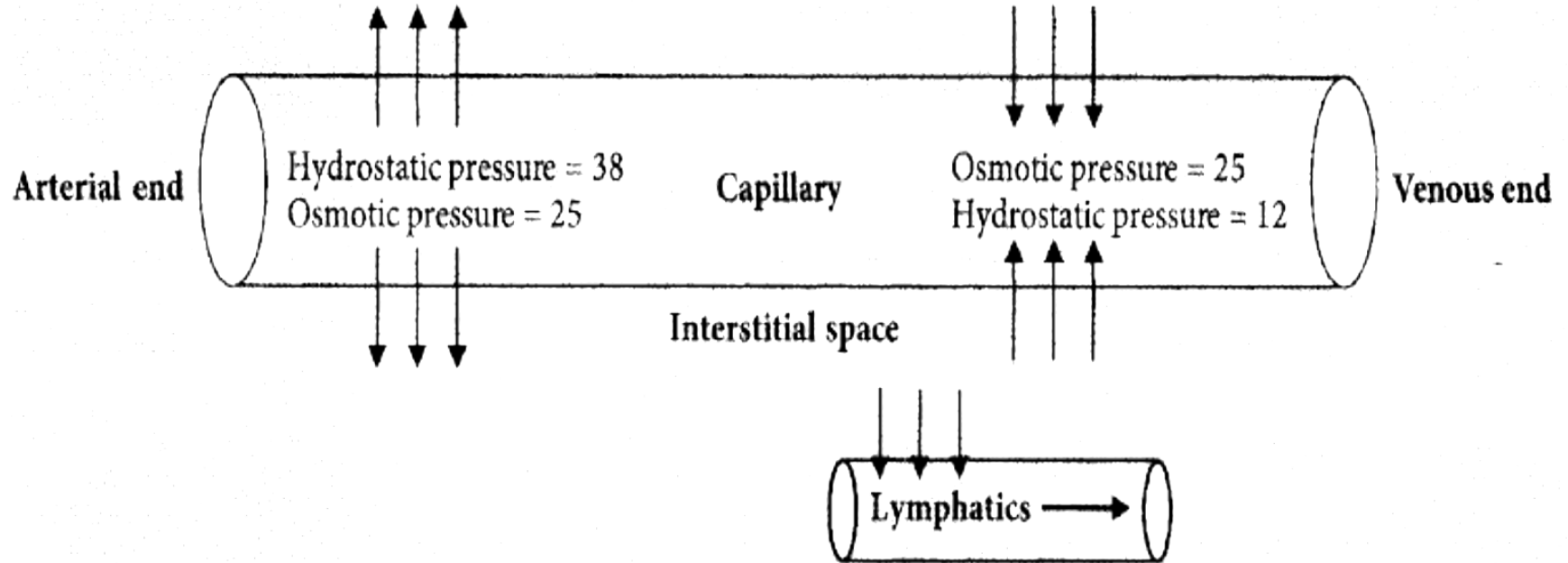




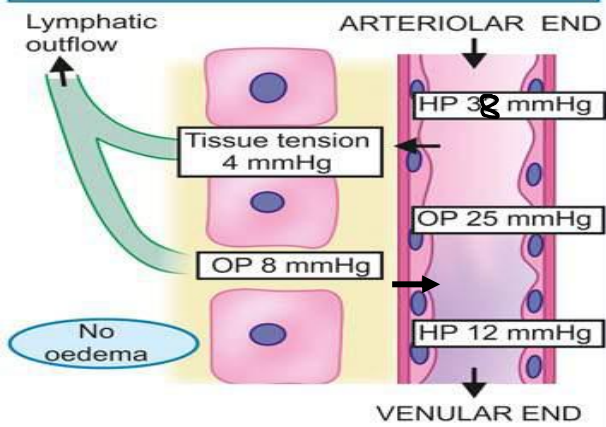
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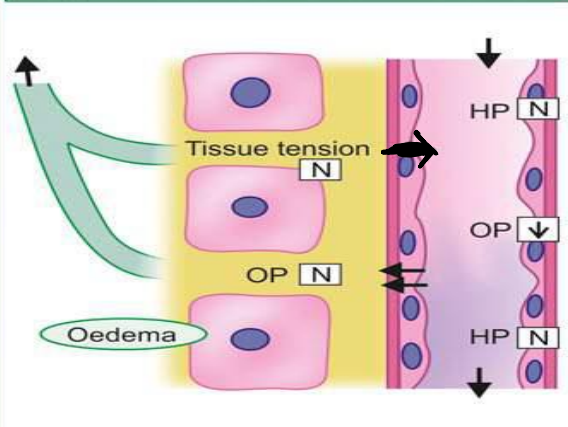
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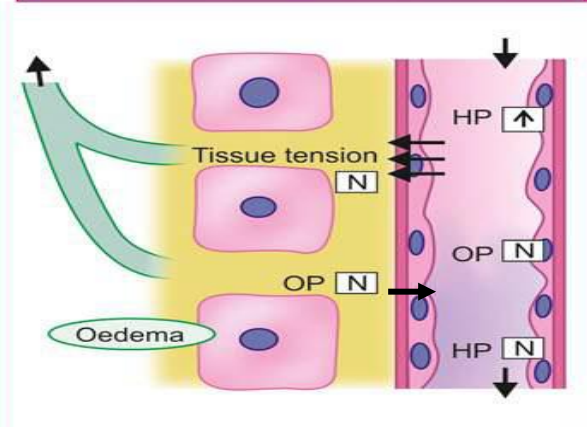
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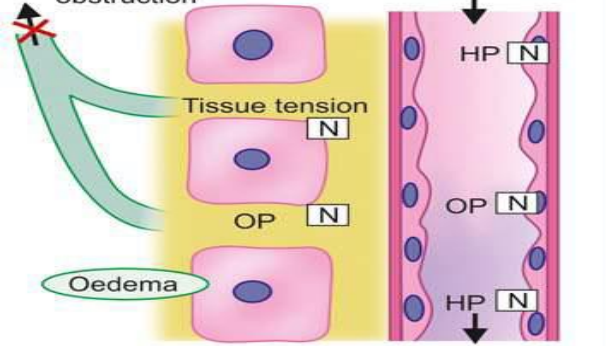
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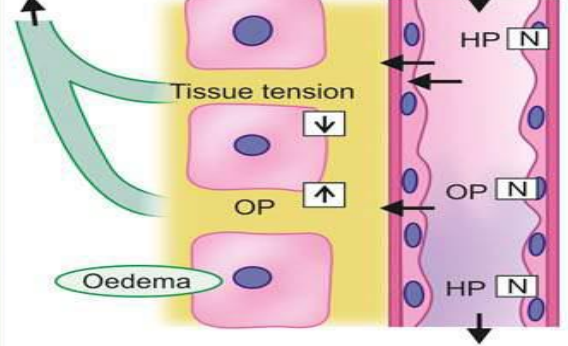
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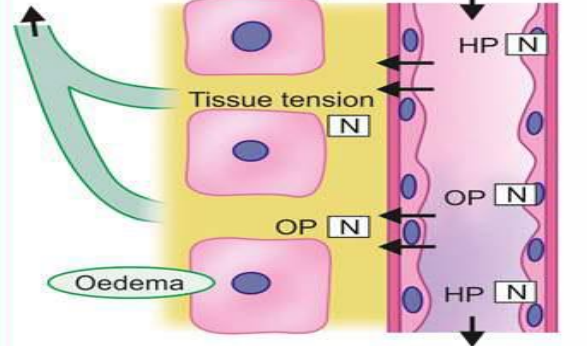
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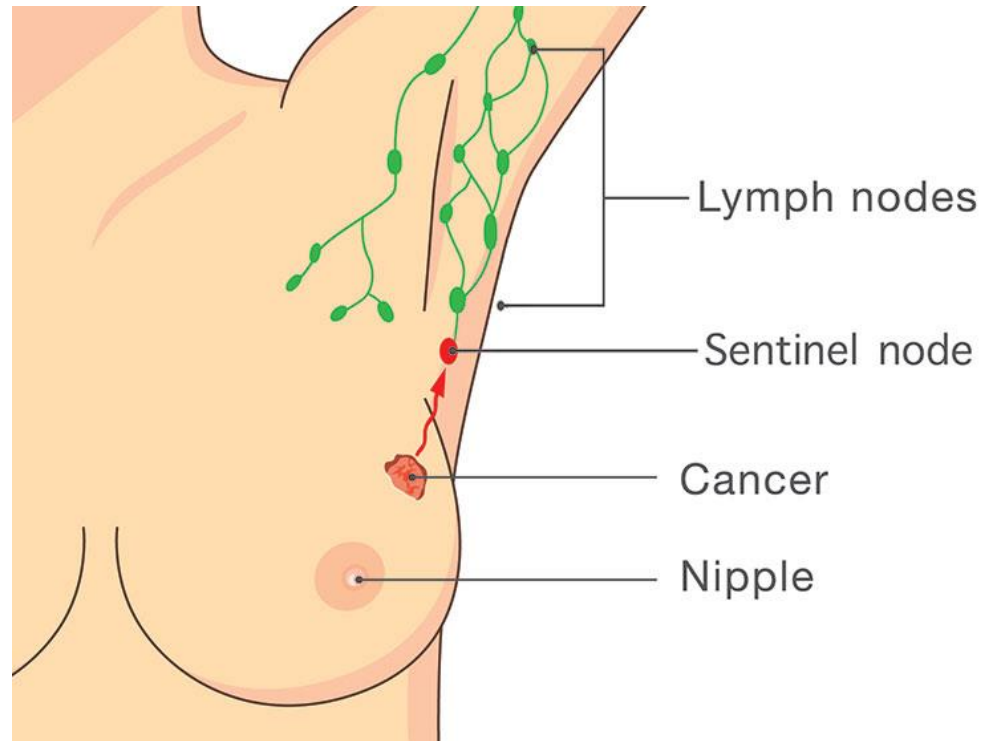


F, ↑ CAPILLARY PERMEABILITY



# Examples →

- 1. Removal of axillary lymph nodes** in radical mastectomy for carcinoma of the breast causing lymphoedema of the affected arm.
- 2. Inflammation of the lymphatics as seen in filariasis (elephantiasis)** results in lymphoedema of scrotum and legs known as elephantiasis
- 3. Milroy's disease or hereditary lymphoedema** is due to abnormal development of lymphatic channels

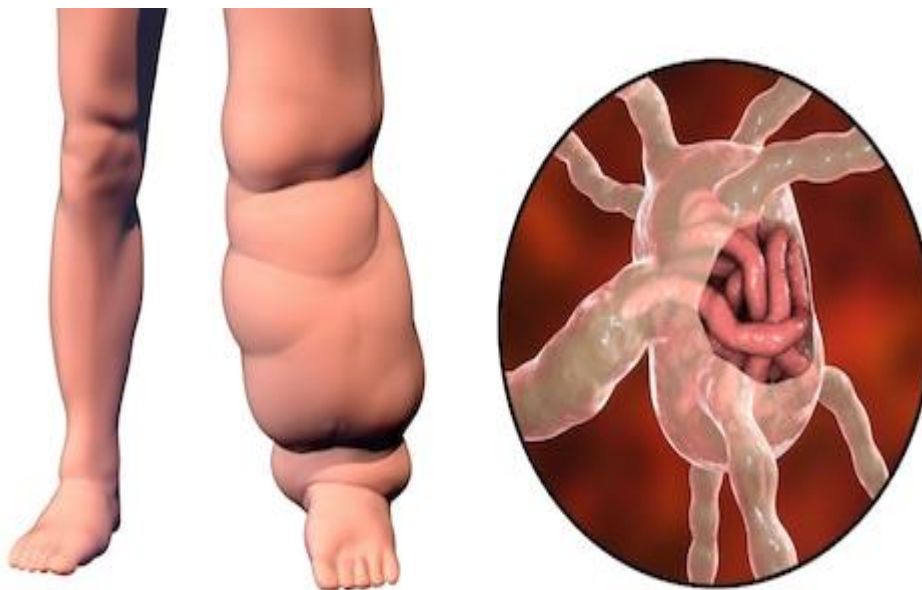




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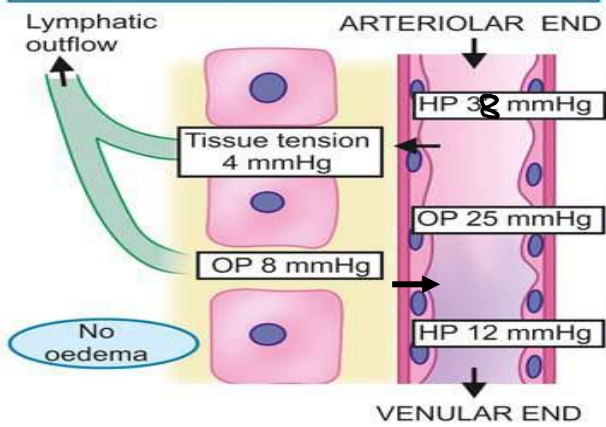
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## **4. Increased oncotic pressure and decreased hydrostatic pressure of the interstitial space**

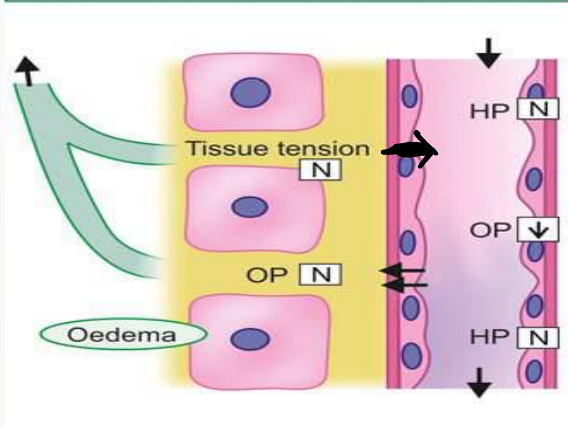
occurs due to →

- Increased vascular permeability
- Inadequate removal of proteins by lymphatics.

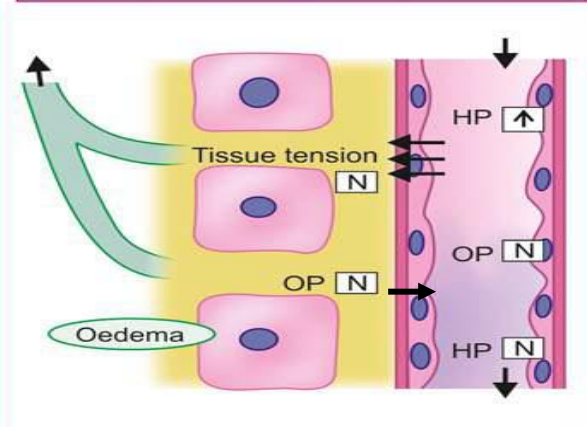
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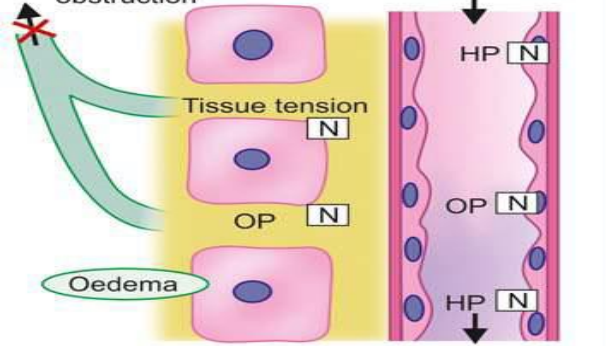
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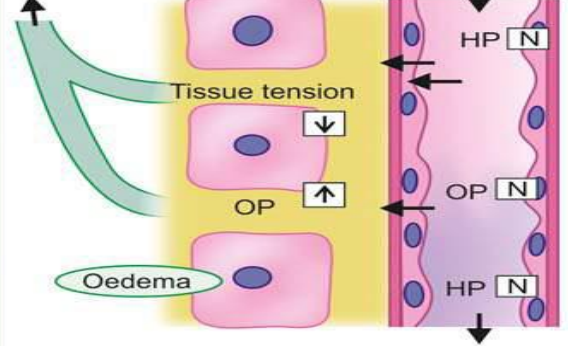
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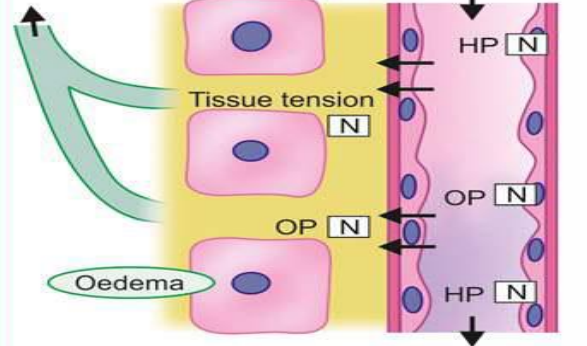
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# **5. SODIUM AND WATER RETENTION**

**Hypovolemia**



**Increased salt retention—with obligate retention of associated water causes both**

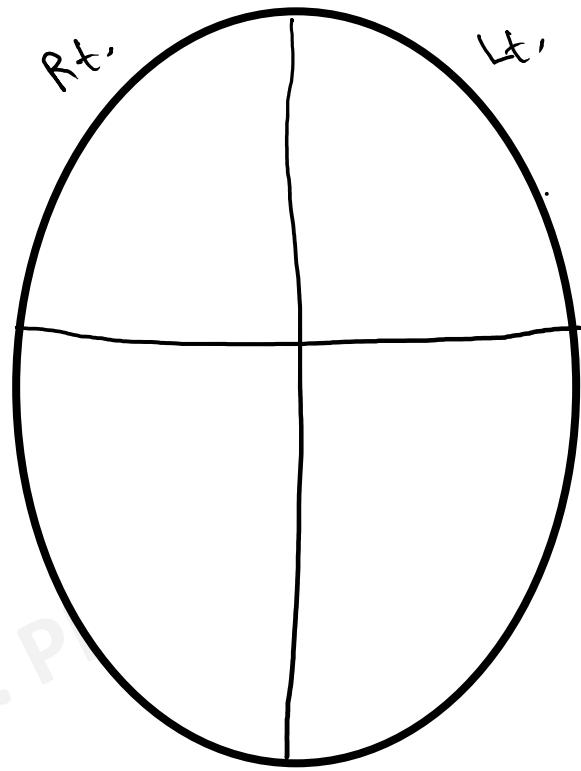


**Increased hydrostatic pressure (due to intravascular fluid volume expansion)**

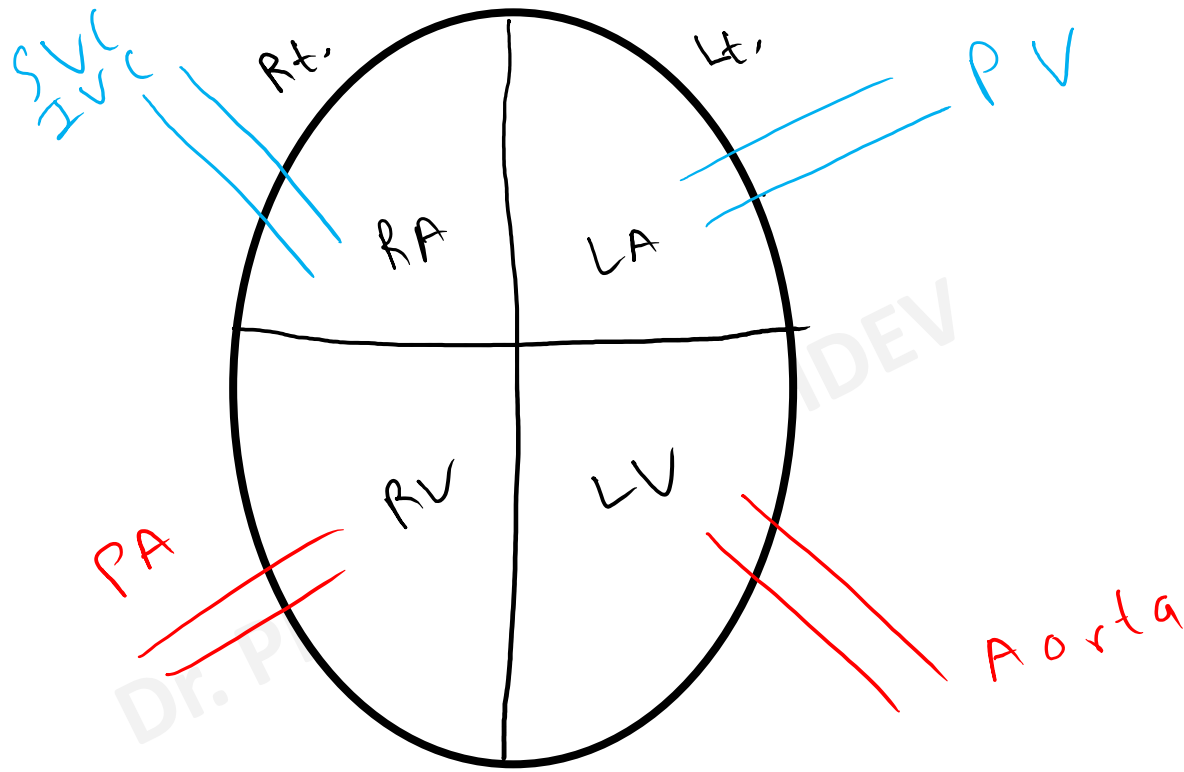
**Diminished vascular colloid osmotic pressure (due to dilution)**

## **Examples →**

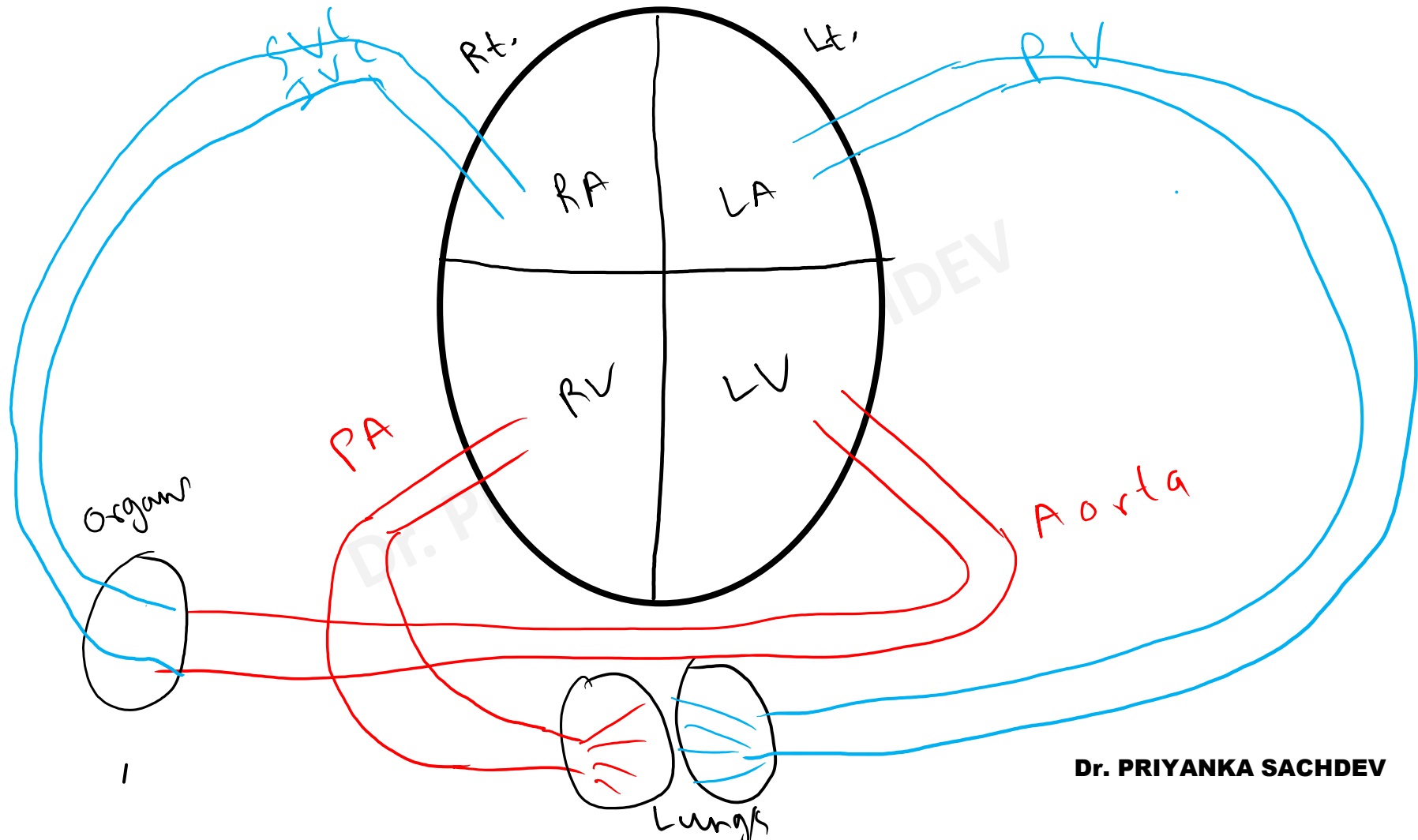
- i) Oedema of cardiac disease e.g. in congestive cardiac failure.
- ii) Oedema of renal disease e.g. in nephrotic and nephritic syndrome.



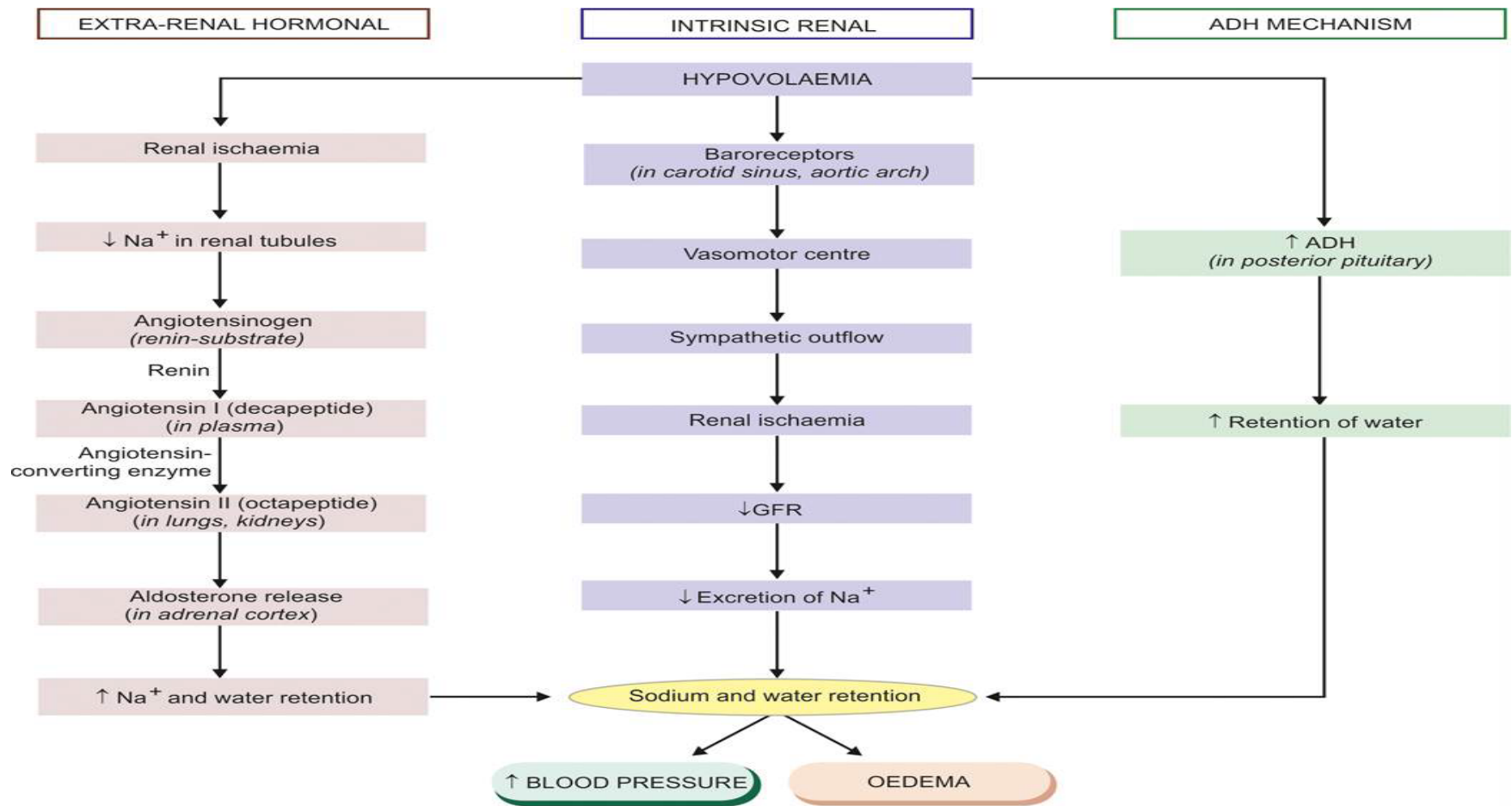
**Dr. PRIYANKA SACHDEV**

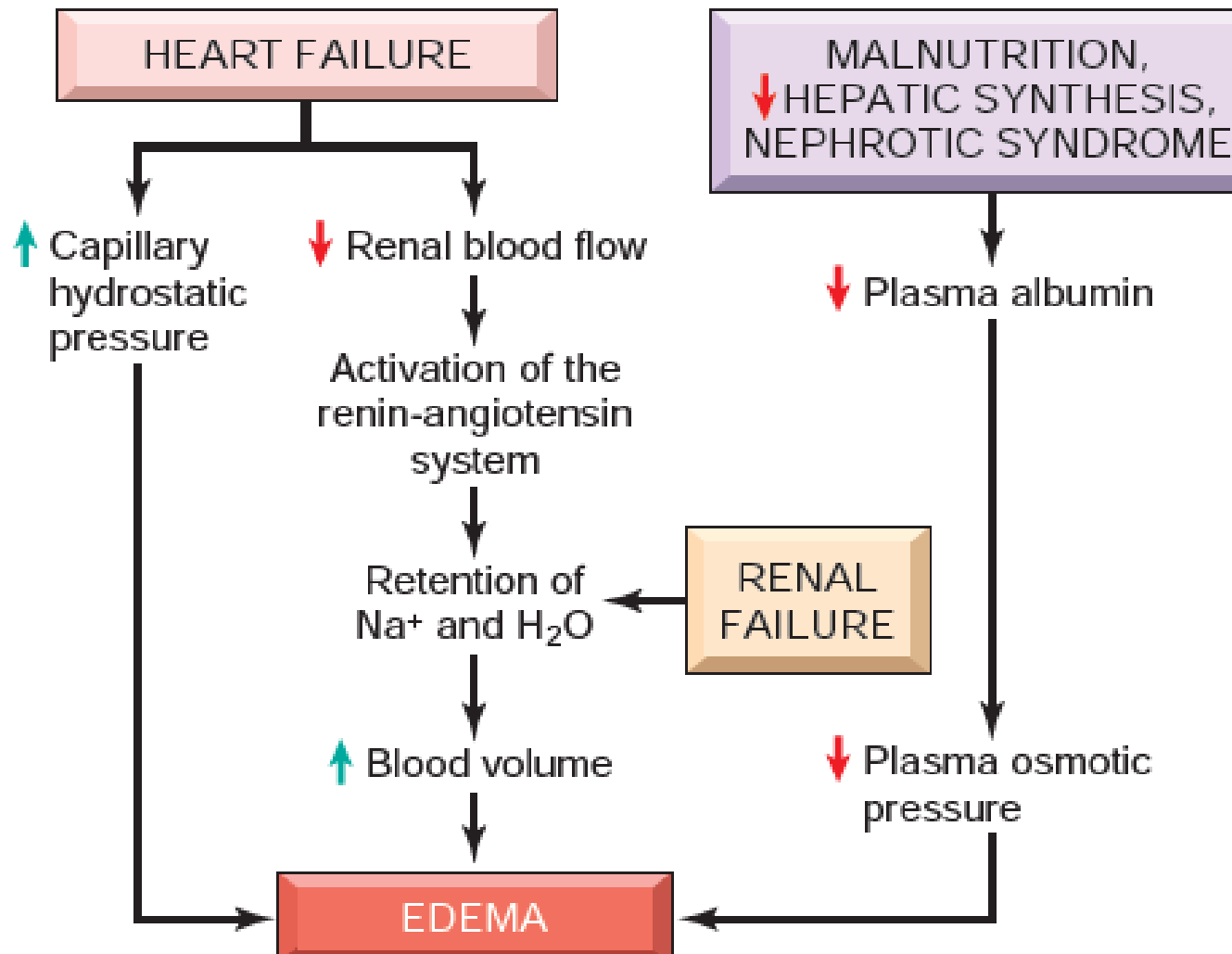






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# **Pathogenesis of edema**

- **1. Increased capillary hydrostatic pressure**
- **2. Decreased plasma oncotic pressure**
- **3. Lymphatic obstruction**
- **4. Tissue factors (increased oncotic pressure of interstitial fluid)**
- **5. Sodium and water retention**
- **6. Increased capillary permeability (Inflammation)**

## **6. INCREASED CAPILLARY PERMEABILITY**

- An intact capillary endothelium is a semipermeable membrane which permits the free flow of water and crystalloids but does not allow passage of plasma proteins normally.

**Capillary endothelium is injured**



**Gaps between the endothelial cells**



**Leakage of plasma proteins into interstitial fluid**

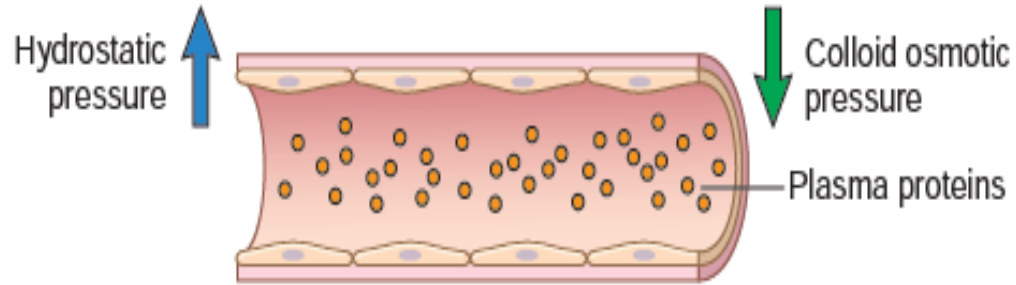


**Reduced plasma oncotic pressure and elevated  
oncotic pressure of interstitial fluid**



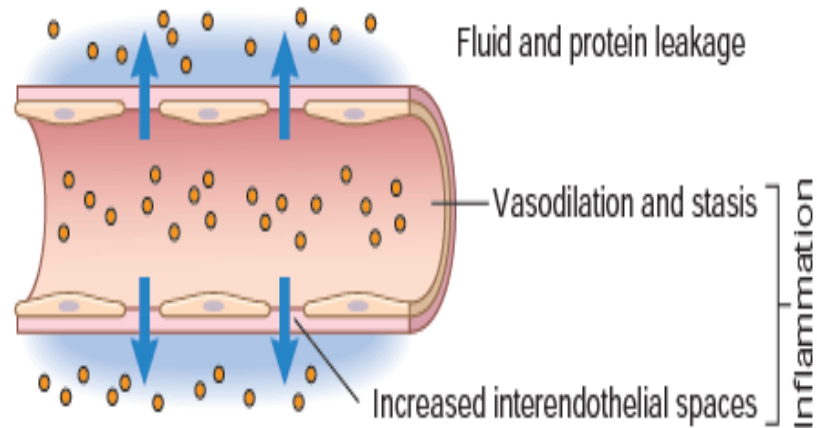
**Oedema**

NORMAL

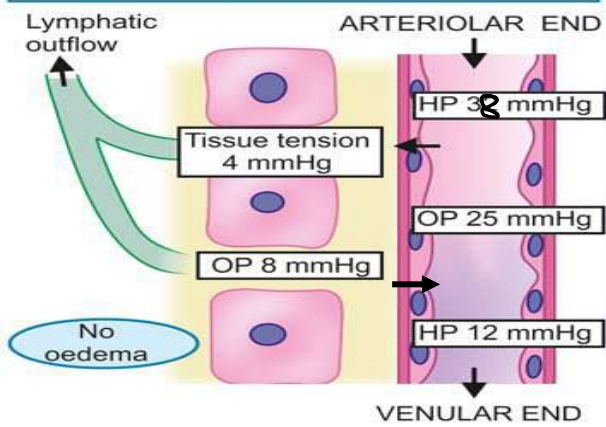


EXUDATE

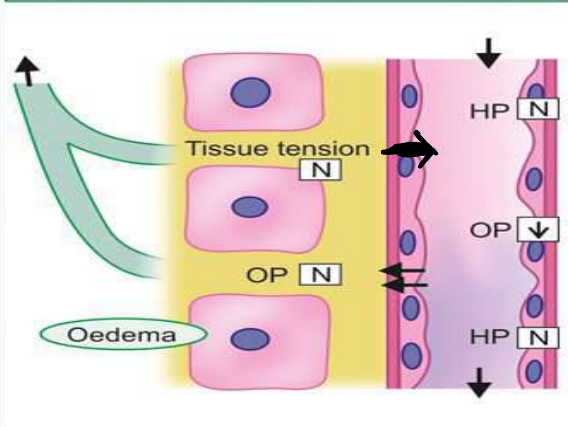
(high protein content, and may contain some white and red cells)



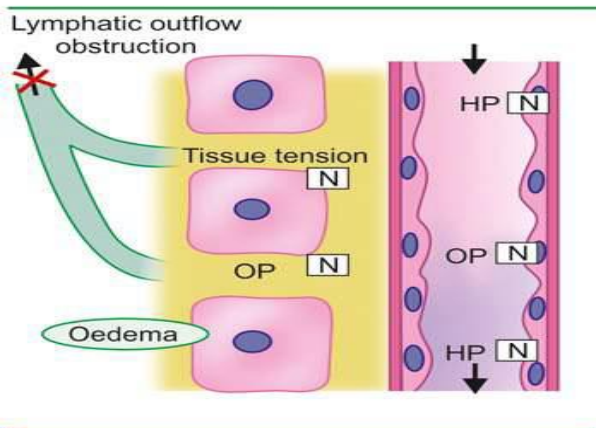
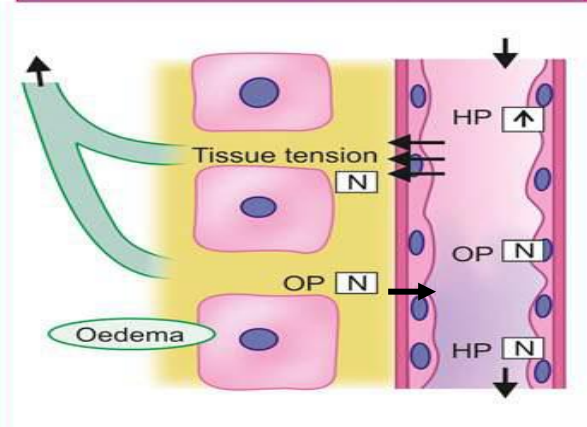
**A, NORMAL FLUID EXCHANGE**



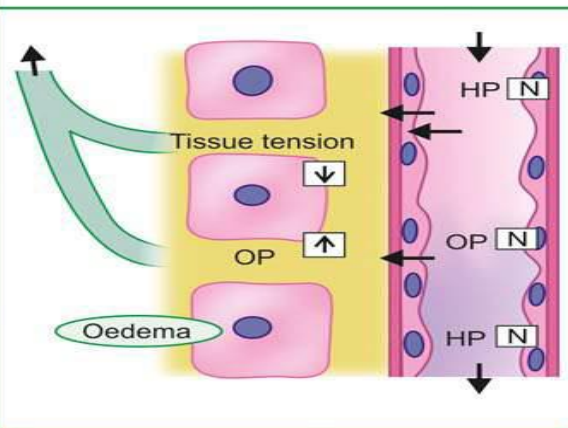
**B, ↓ PLASMA OSMOTIC PRESSURE**



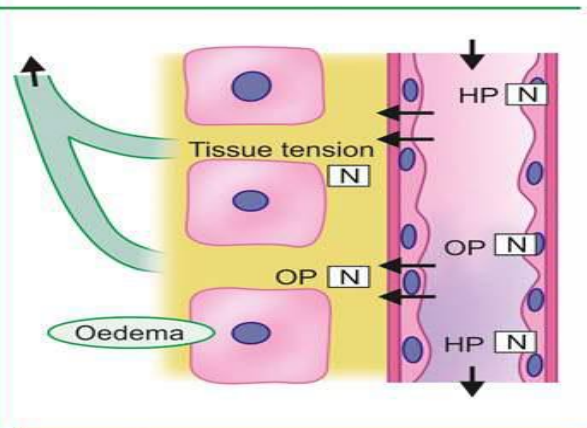
**C, ↑ CAPILLARY PRESSURE**



**D, LYMPHOEDEMA**



**E, TISSUE FACTORS**

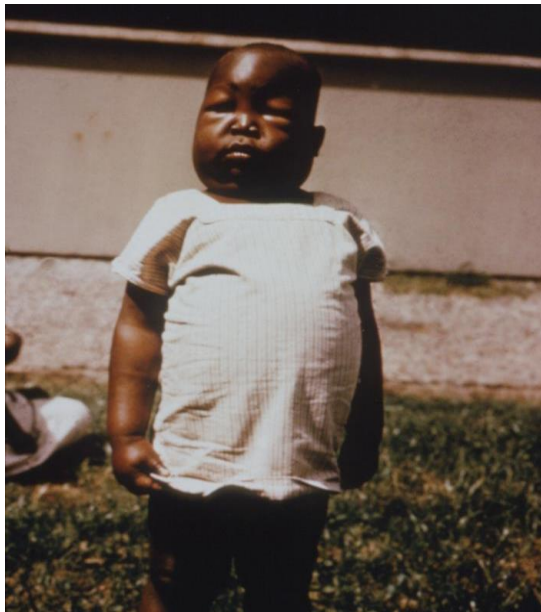


**F, ↑ CAPILLARY PERMEABILITY**



# Examples

- **i) Generalised oedema** occurring in systemic infections, poisonings, certain drugs and chemicals, anaphylactic reactions and anoxia.
- **ii) Localised oedema** due to allergic reactions, insect-bite, irritant drugs and chemicals.



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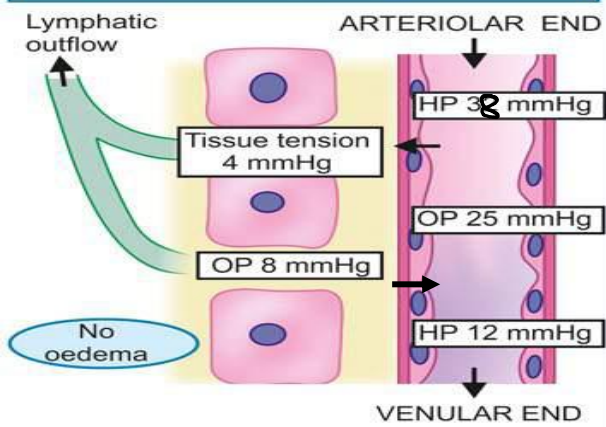
# **Pathogenesis of edema**

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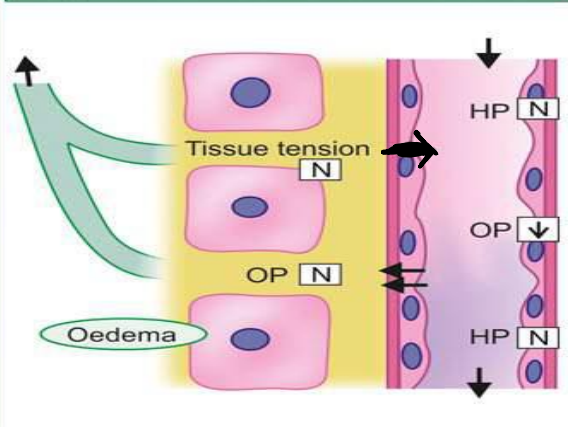
## Causes and conditions associated with edema

↑ Hydrostatic pressure	↓ Plasma osmotic pressure	Lymphatic obstruction (Lymphedema)	Sodium retention	Inflammation
<ul style="list-style-type: none"><li>• CHF</li><li>• Ascites (Cirrhosis)</li><li>• Venous obstruction due to thrombosis of physical inactivity</li><li>• Arteriolar dilation</li></ul>	<ul style="list-style-type: none"><li>• Liver cirrhosis</li><li>• Malnutrition</li><li>• Protein-losing gastroenteropathy</li></ul>	<ul style="list-style-type: none"><li>• After surgery or irradiation</li><li>• Neoplasia</li><li>• Inflammatory</li></ul>	<ul style="list-style-type: none"><li>• ↑ Salt intake</li><li>• ↓ Renal perfusion</li><li>• ↑ RAAS activity</li></ul>	<ul style="list-style-type: none"><li>• Acute and chronic inflammation</li></ul>

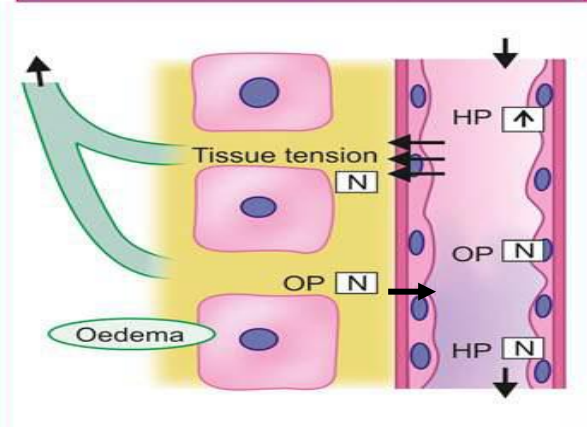
**A, NORMAL FLUID EXCHANGE**



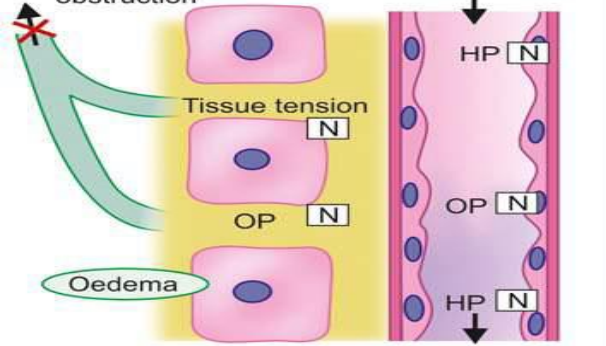
**B, ↓ PLASMA OSMOTIC PRESSURE**



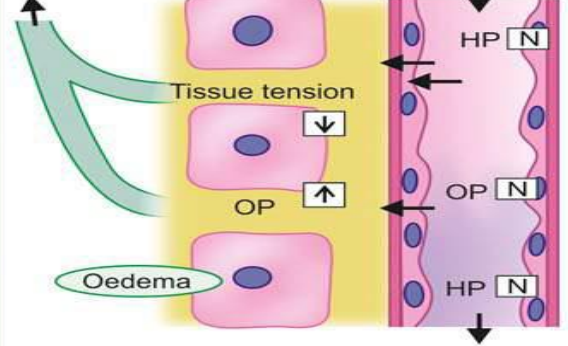
**C, ↑ CAPILLARY PRESSURE**



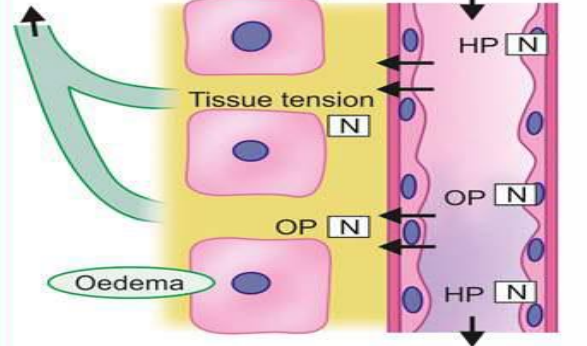
**D, Lymphoedema**



**E, TISSUE FACTORS**



**F, ↑ CAPILLARY PERMEABILITY**

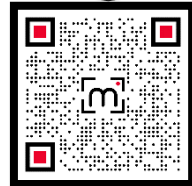


# **OVERVIEW**

- **Definition**
- **Normal tissue exchange**
- **Pathogenesis**
- **Types of oedema fluid**
- **Important types of oedema**

# Types of edema fluid

*Click or Scan QR code to join  
Telegram group discussion*



med[LIVE]

- **Transudate** is protein-poor and cell-poor fluid.

- **Exudate** is protein-rich and cell-rich fluid.



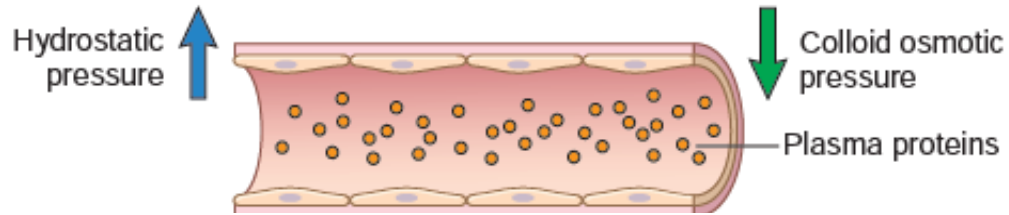
## TRANSUDATE

- A transudate is a fluid with **low protein content** and a specific gravity of less than 1.012.
- It is essentially an ultrafiltrate of blood plasma that results from osmotic or hydrostatic imbalance across the vessel wall without an increase in vascular permeability.

## EXUDATE

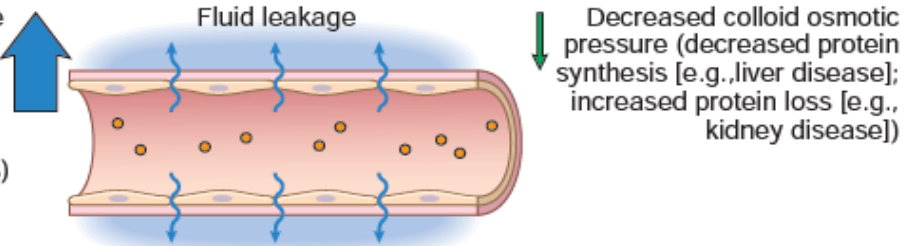
- An exudate is an inflammatory extravascular fluid that has a **high protein concentration**, cellular debris, and a specific gravity above 1.020.
- It is formed mainly due to alteration in the normal permeability of small blood vessels in the area of injury.

NORMAL

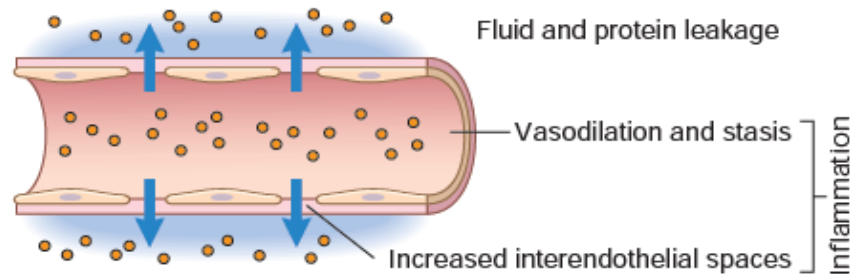


Increased hydrostatic pressure  
(venous outflow obstruction,  
[e.g., congestive heart failure])

TRANSUDATE  
(low protein content, few cells)



EXUDATE  
(high protein content, and  
may contain some white  
and red cells)



FEATURE	TRANSUDATE	EXUDATE
1. <i>Definition</i>	Filtrate of blood plasma without changes in endothelial permeability	Oedema of inflamed tissue associated with increased vascular permeability
2. <i>Character</i>	Non-inflammatory oedema	Inflammatory oedema
3. <i>Protein content</i>	Low (less than 1 gm/dl); mainly albumin, low fibrinogen; hence no tendency to coagulate	High ( 2.5-3.5 gm/dl), readily coagulates due to high content of fibrinogen and other coagulation factors
4. <i>Glucose content</i>	Same as in plasma	Low (less than 60 mg/dl)
5. <i>Specific gravity</i>	Low (less than 1.015)	High (more than 1.018)
6. <i>pH</i>	> 7.3	< 7.3
7. <i>LDH</i>	Low	High
8. <i>Effusion LDH/ Serum LDH ratio</i>	< 0.6	> 0.6
9. <i>Cells</i>	Few cells, mainly mesothelial cells and cellular debris	Many cells, inflammatory as well as parenchymal
10. <i>Examples</i>	Oedema in congestive cardiac failure	Purulent exudate such as pus

# REMEMBER

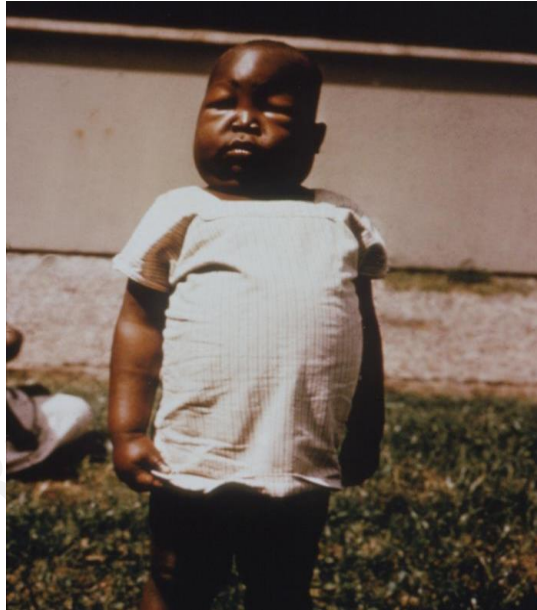
1. Severe generalized edema is called **anasarca**.

2. When edema is influenced by gravity, it is called **dependent edema**

- (e.g., it appears in the legs when standing and the sacrum when recumbent),
- It is a characteristic feature of **congestive heart failure**

3. Edema due to a **renal cause (as in Nephrotic syndrome)** is more severe and affects all parts of body.

- It is initially appreciated in tissue with loose tissue matrix such as around eyes and is called **periorbital edema**



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# REMEMBER

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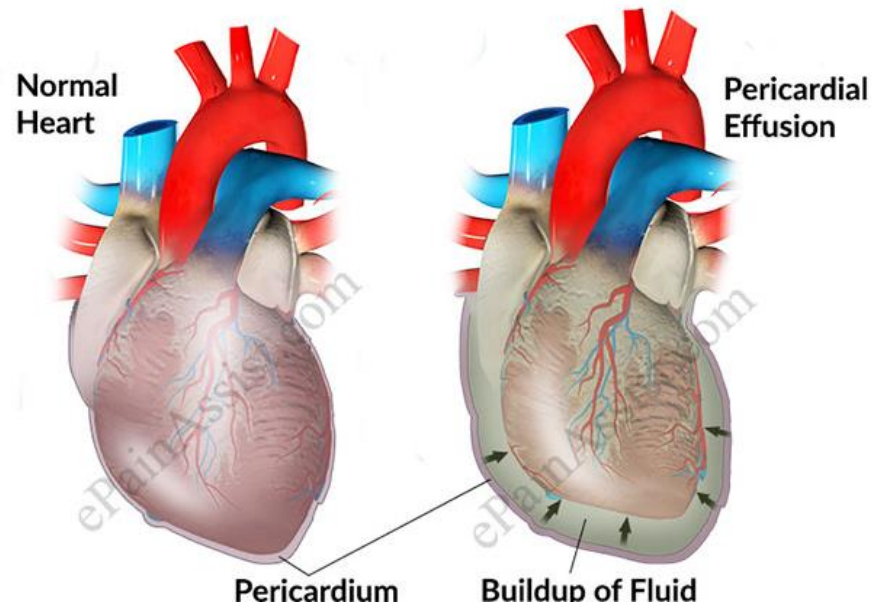
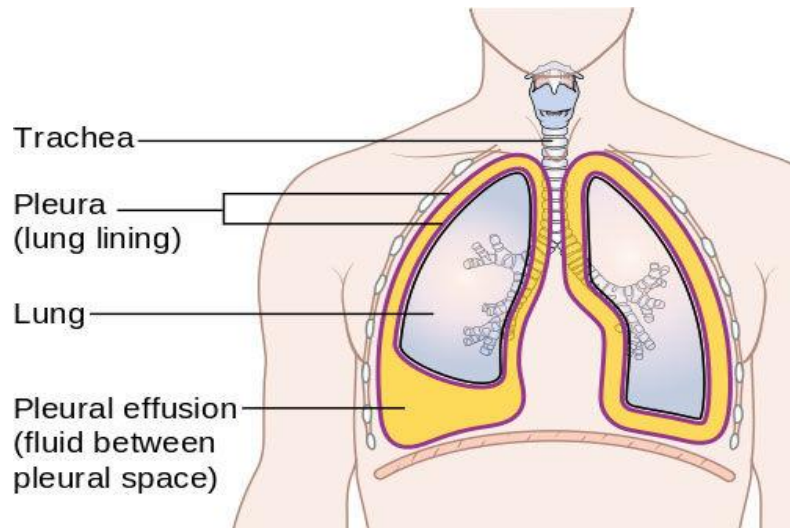


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# Effusions

- Involving the pleural cavity (**hydrothorax**)
- Involving the pericardial cavity (**hydropericardium**)
- Involving the peritoneal cavity (**hydroperitoneum or ascites**)

- ✓ **Transudative effusions** are typically protein-poor, translucent and straw colored
- ✓ **Exudative effusions** are protein-rich and often cloudy due to the presence of white cells.



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# OVERVIEW

- Definition
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- Pathogenesis
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- Important types of oedema

# IMPORTANT TYPES OF OEDEMA



# **IMPORTANT TYPES OF OEDEMA**

- **Renal Oedema**
- **Cardiac Oedema**
- **Pulmonary Oedema**
- **Myxoedema**
- **Hepatic Oedema**

# **Renal Oedema**

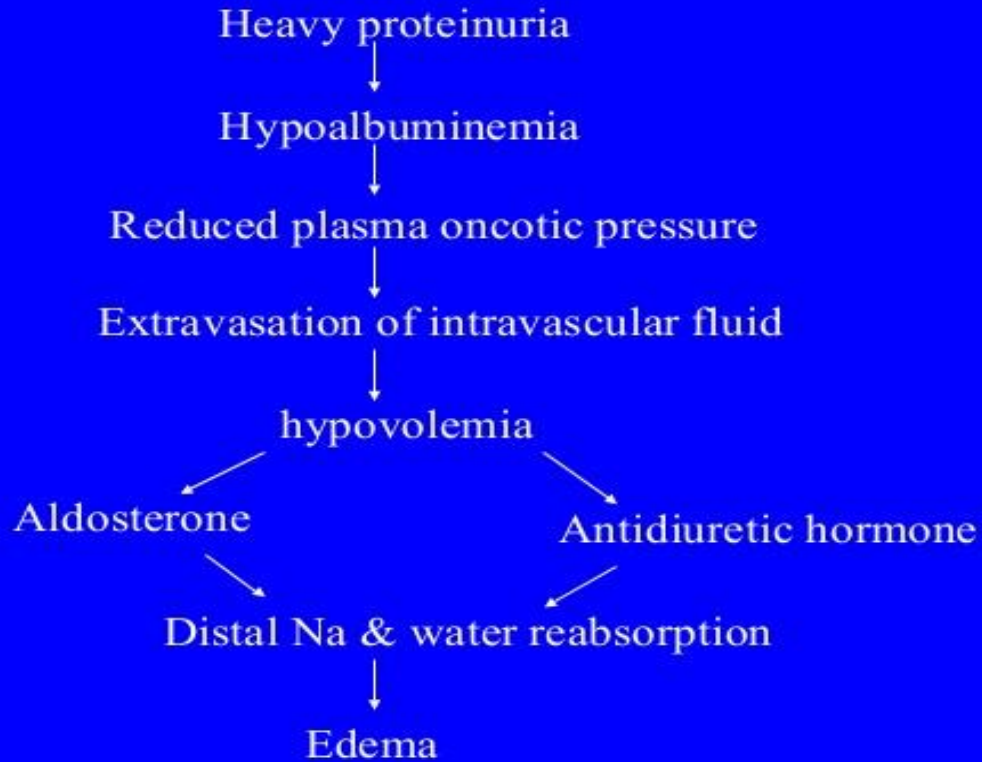
- **1. Oedema in nephrotic syndrome**
- **2. Oedema in nephritic syndrome**

# 1. Oedema in nephrotic syndrome

- The nephrotic oedema is **severe** as compared to nephritic oedema
- Oedema is **generalised**



# Pathophysiology



**Nephrotic syndrome**



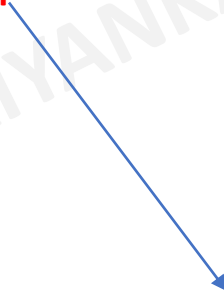
**persistent and heavy proteinuria (albuminuria)**



**Hypoalbuminaemia**



**Decreased plasma oncotic pressure**



**Fall in the plasma volume**



**RAS activated**



**Retention of sodium and water**



**Odema**

## 2. Oedema in nephritic syndrome

- The nephritic oedema is usually **mild** as compared to nephrotic oedema
- Oedema begins in the **loose tissues such as on the face around eyes, ankles and genitalia.**

**Nephritic syndrome**



**Renal ischemia**



**RAS activated**



**Retention of sodium and water**



**Odema**

# Renal Oedema

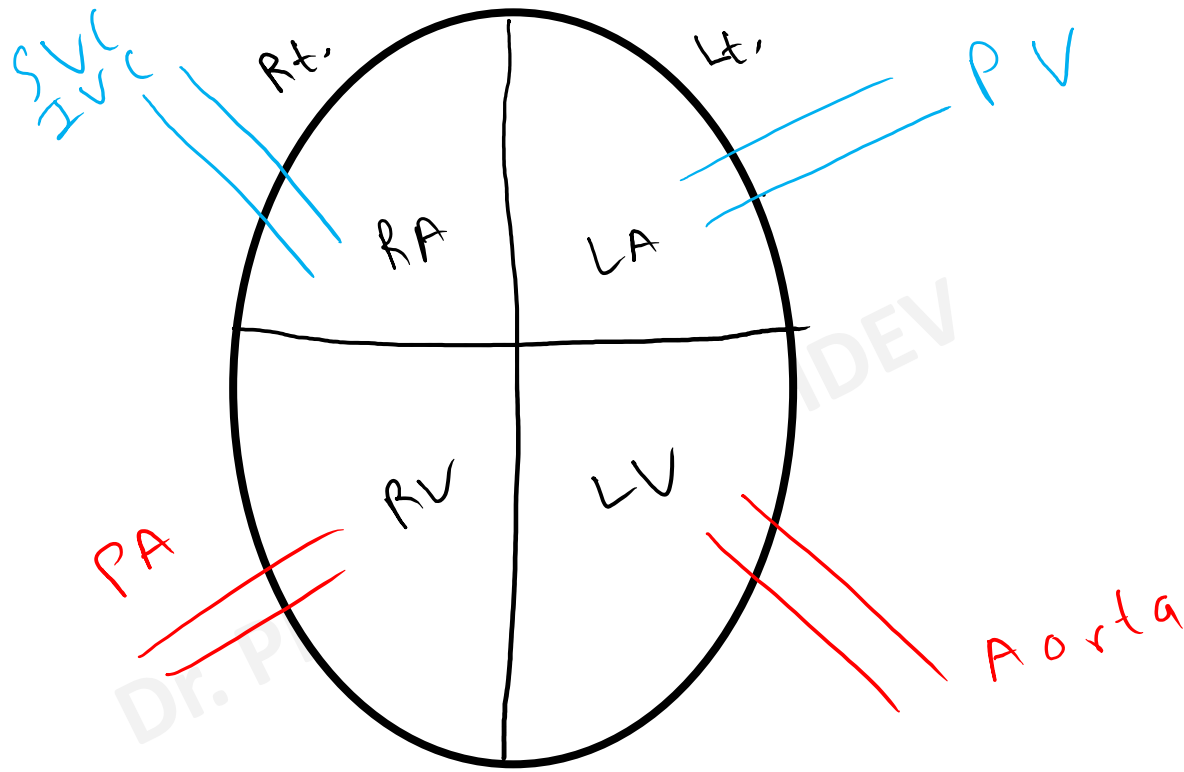
FEATURE	NEPHROTIC OEDEMA	NEPHRITIC OEDEMA
1. Cause	Nephrotic syndrome	Glomerulonephritis (acute, rapidly progressive)
2. Proteinuria	Heavy	Moderate
3. Protein content	High (>1 g/dl)	Low (<0.5 g/dl)
4. Mechanism	↓ Plasma oncotic pressure, Na <sup>+</sup> and water retention	Na <sup>+</sup> and water retention
5. Degree of oedema	Severe, generalised	Mild
6. Distribution	Subcutaneous tissues as well as visceral organs	Loose tissues mainly (face, eyes, ankles, genitalia)

# **IMPORTANT TYPES OF OEDEMA**

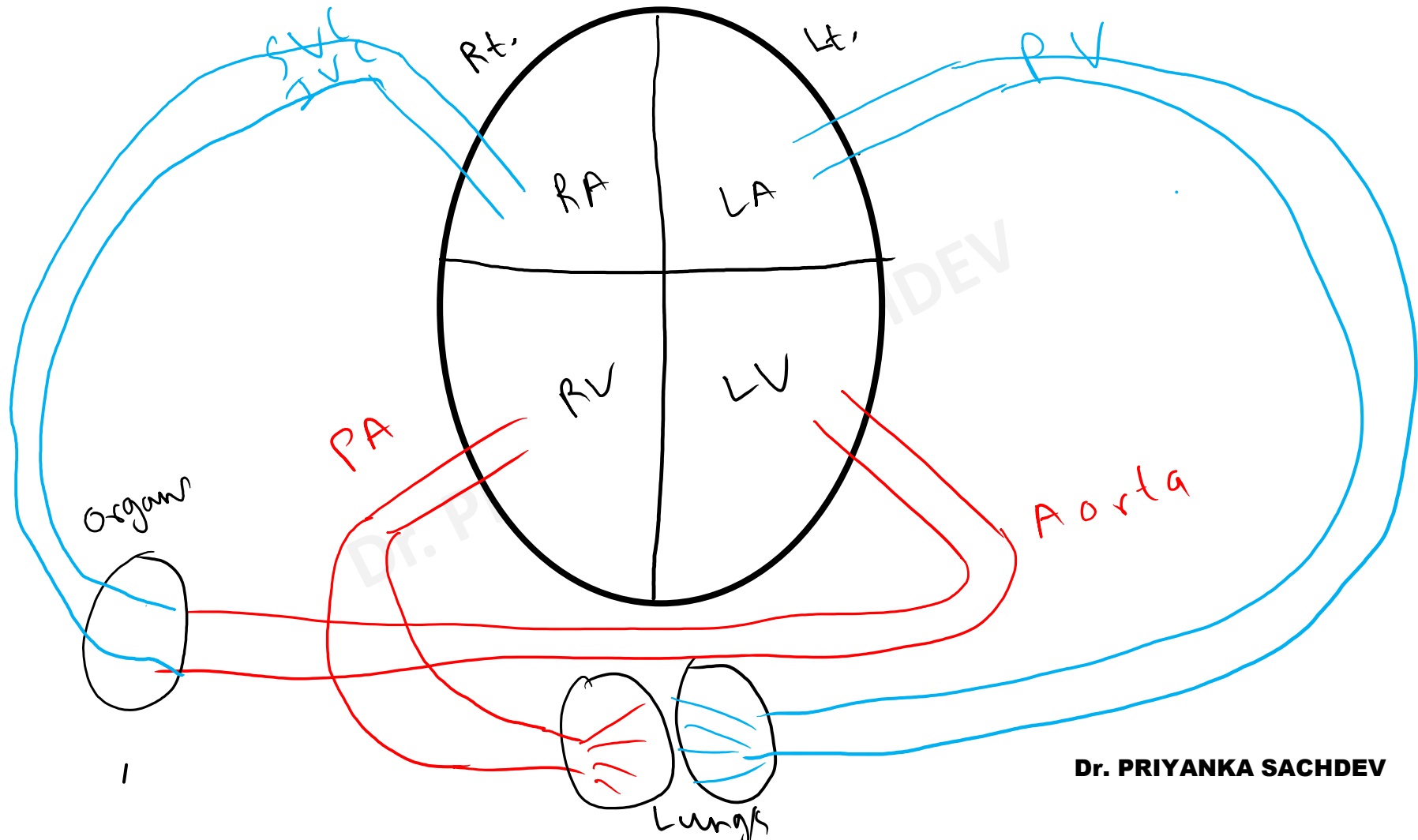
- **Renal Oedema**
- **Cardiac Oedema**
- **Pulmonary Oedema**
- **Myxoedema**
- **Hepatic Oedema**

# Cardiac Oedema

- **Generalised oedema** develops in **congestive cardiac failure.**
- **Pulmonary oedema** develops in **left-sided cardiac failure.**





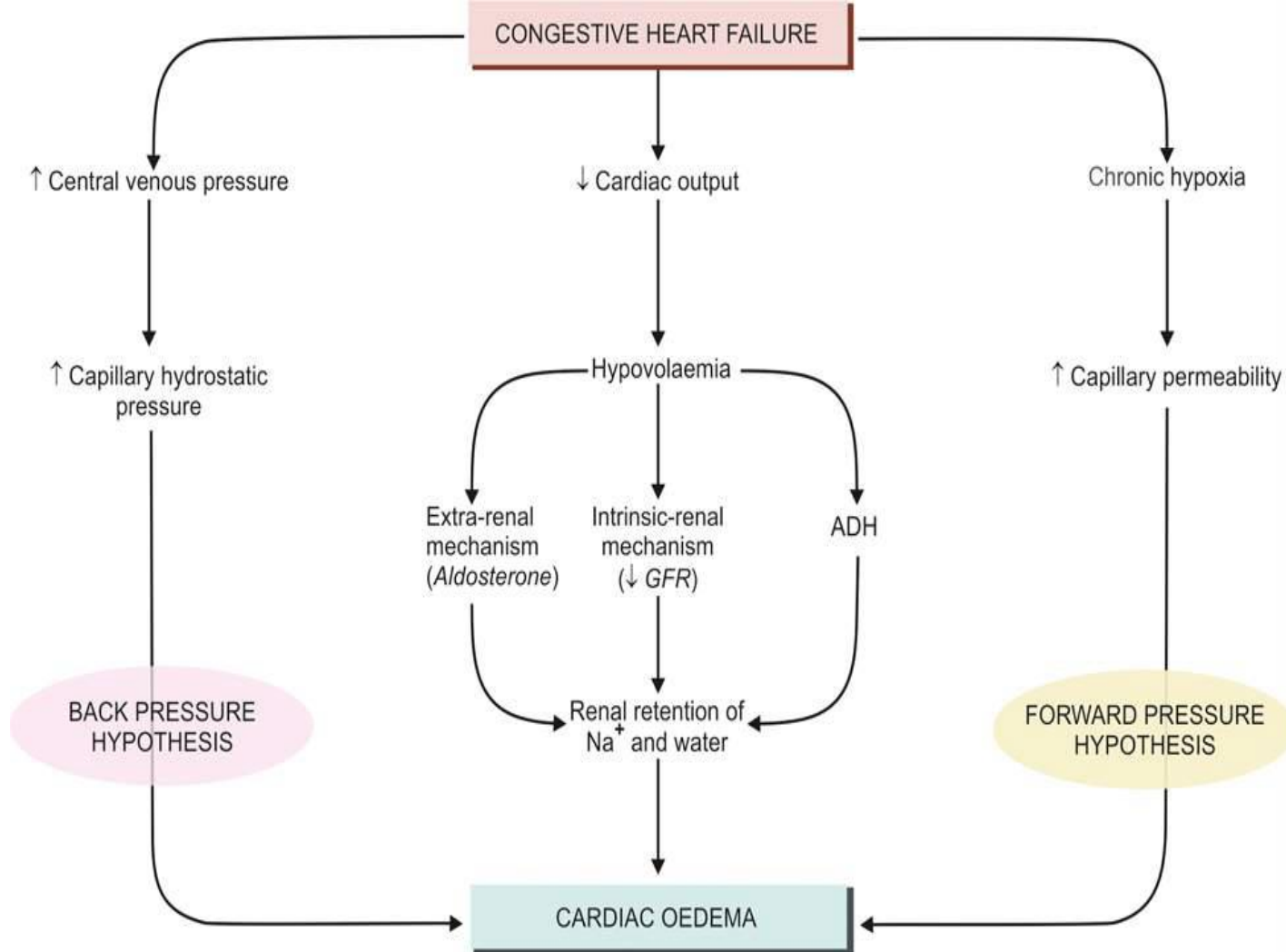


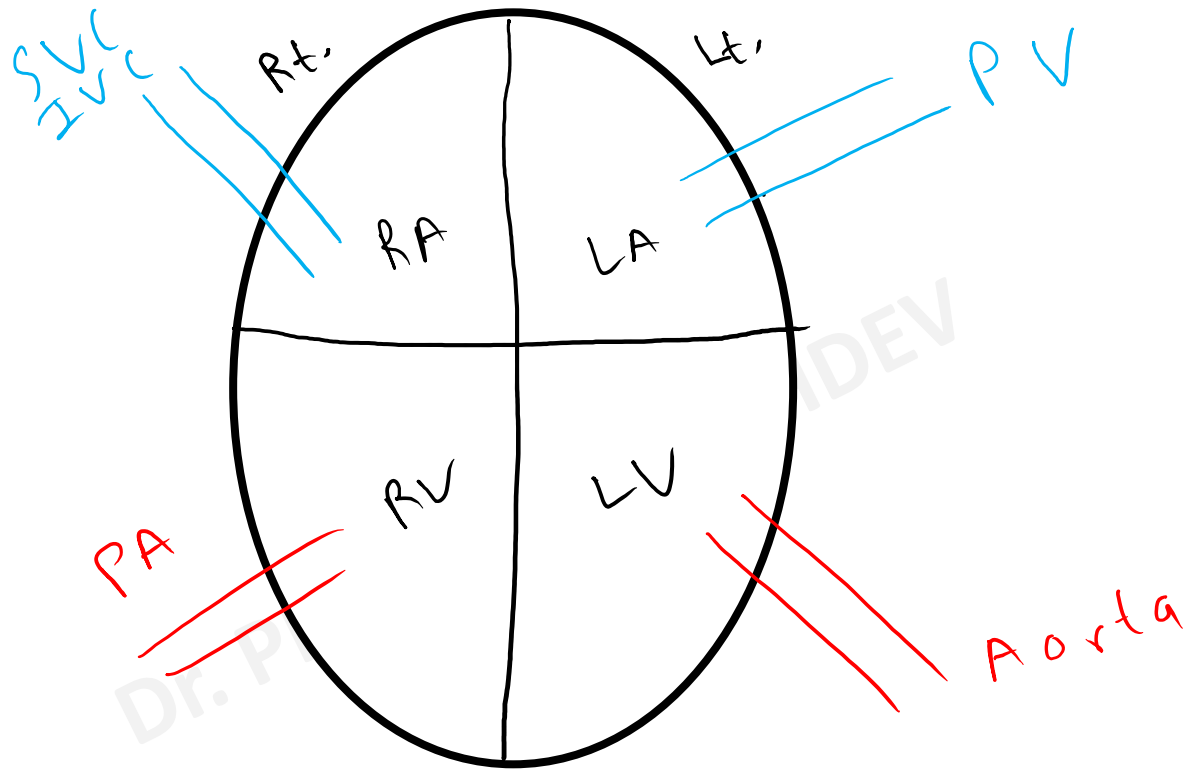
# Congestive cardiac failure

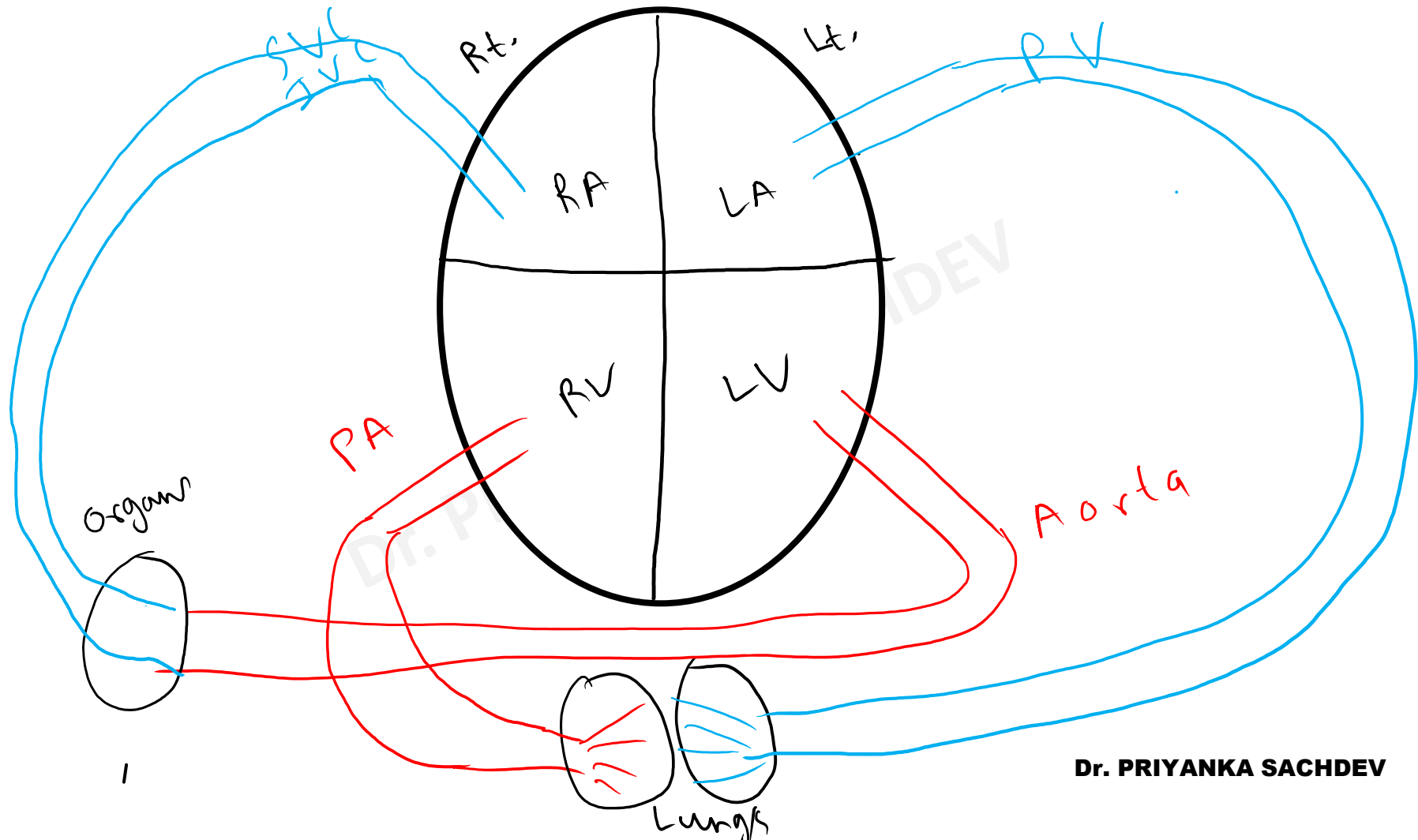
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**Reduced cardiac output**



**Hypovolaemia**



**Renal ischemia**



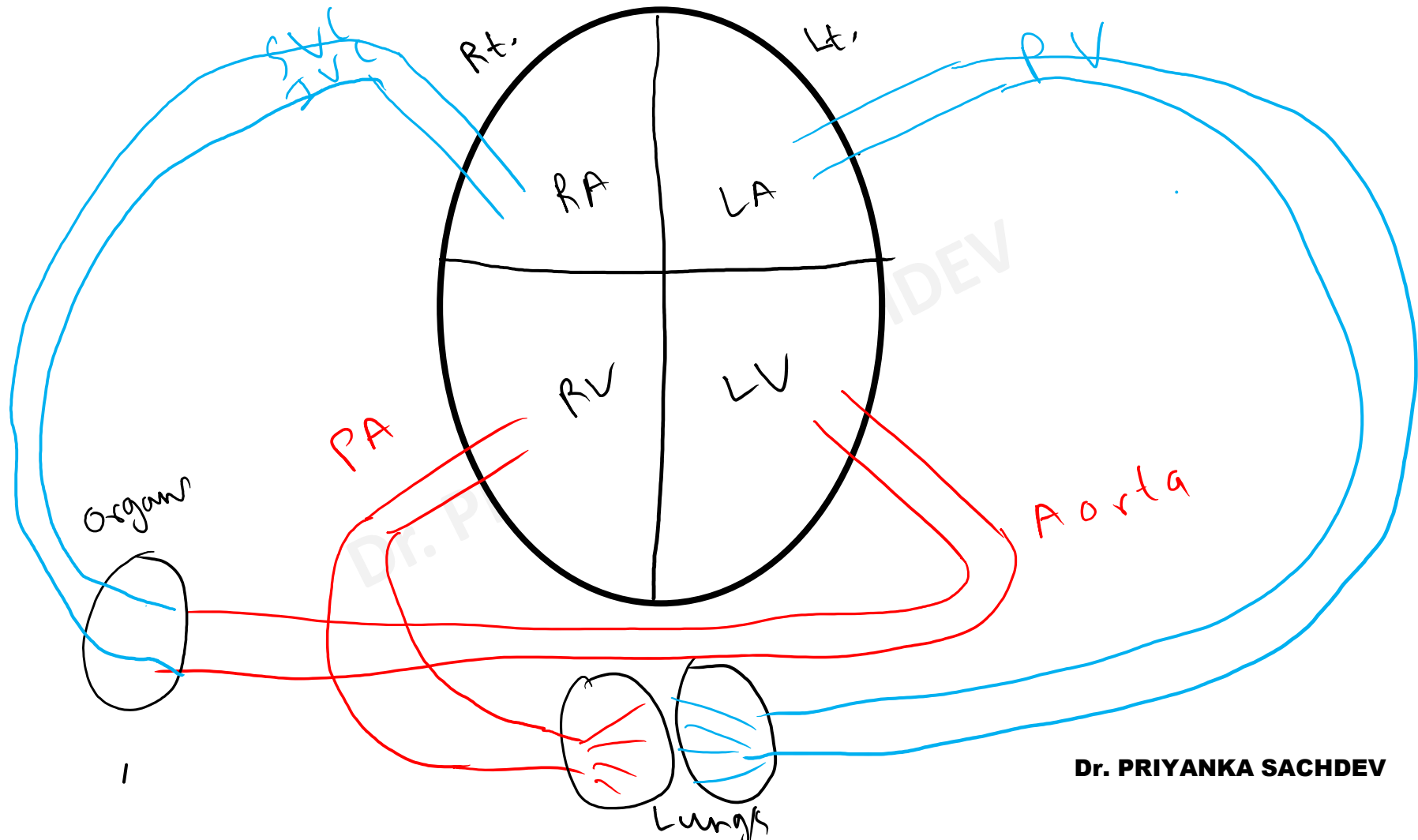
**stimulates RAS mechanisms as well as ADH secretion**



**Sodium and water retention**



**Oedema**



# Back pressure hypothesis

Right Heart failure



Elevated central venous pressure



This pressure transmitted backward to the venous end of the capillaries,

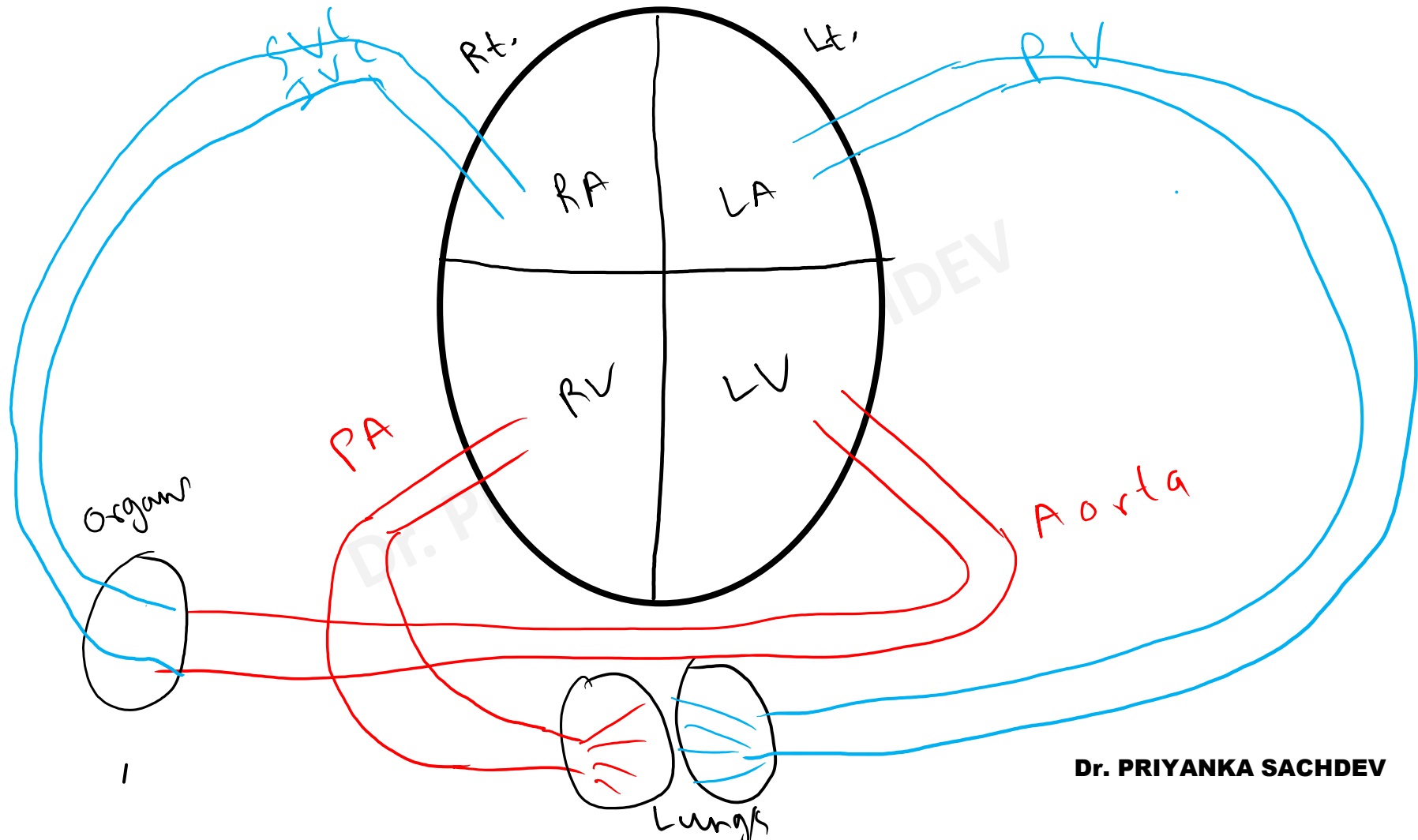


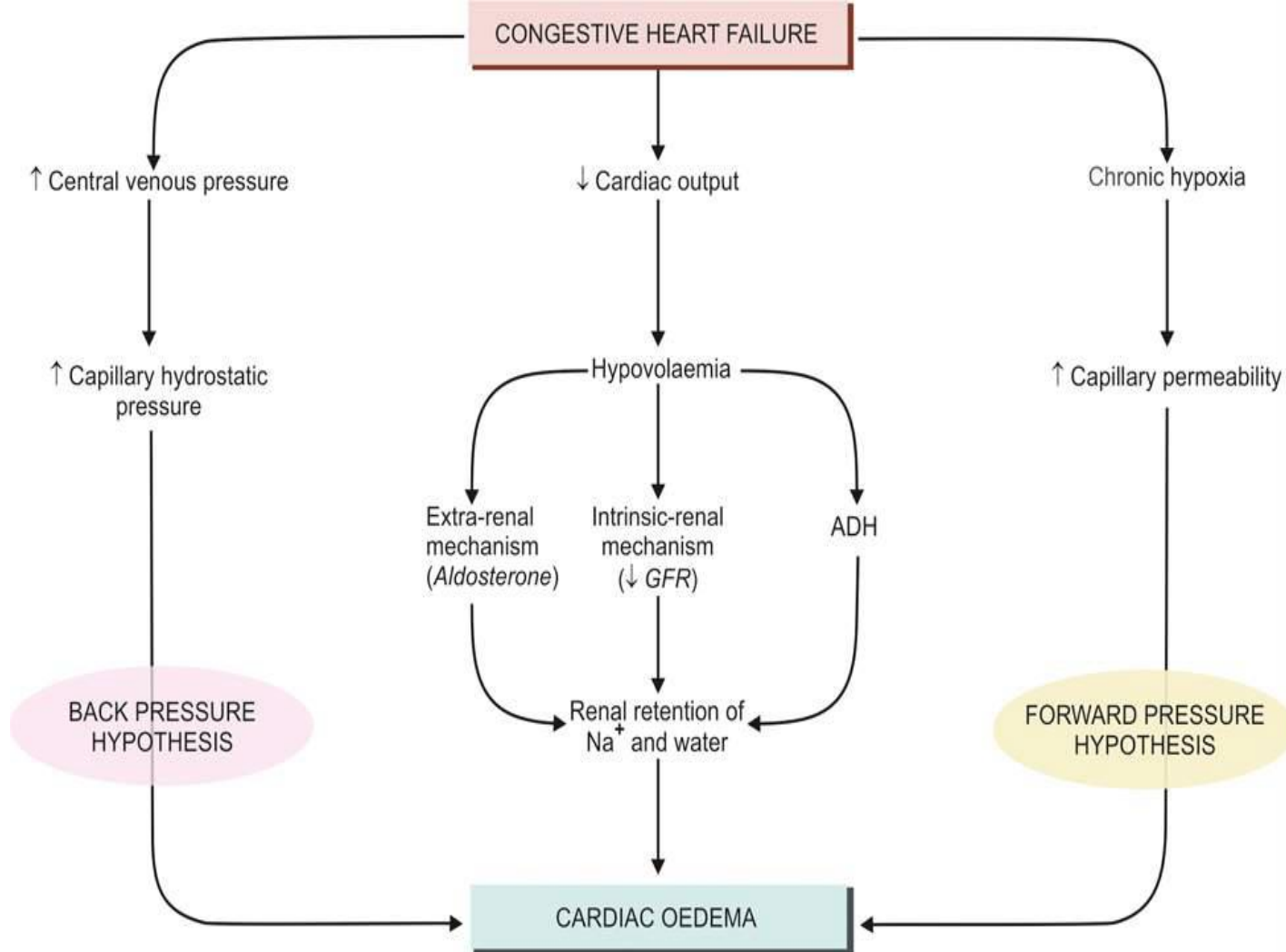
**raising the capillary hydrostatic pressure**



Odema







# Forward pressure hypothesis

Reduced cardiac output



Chronic hypoxia to tissue



Injure the capillary endothelium

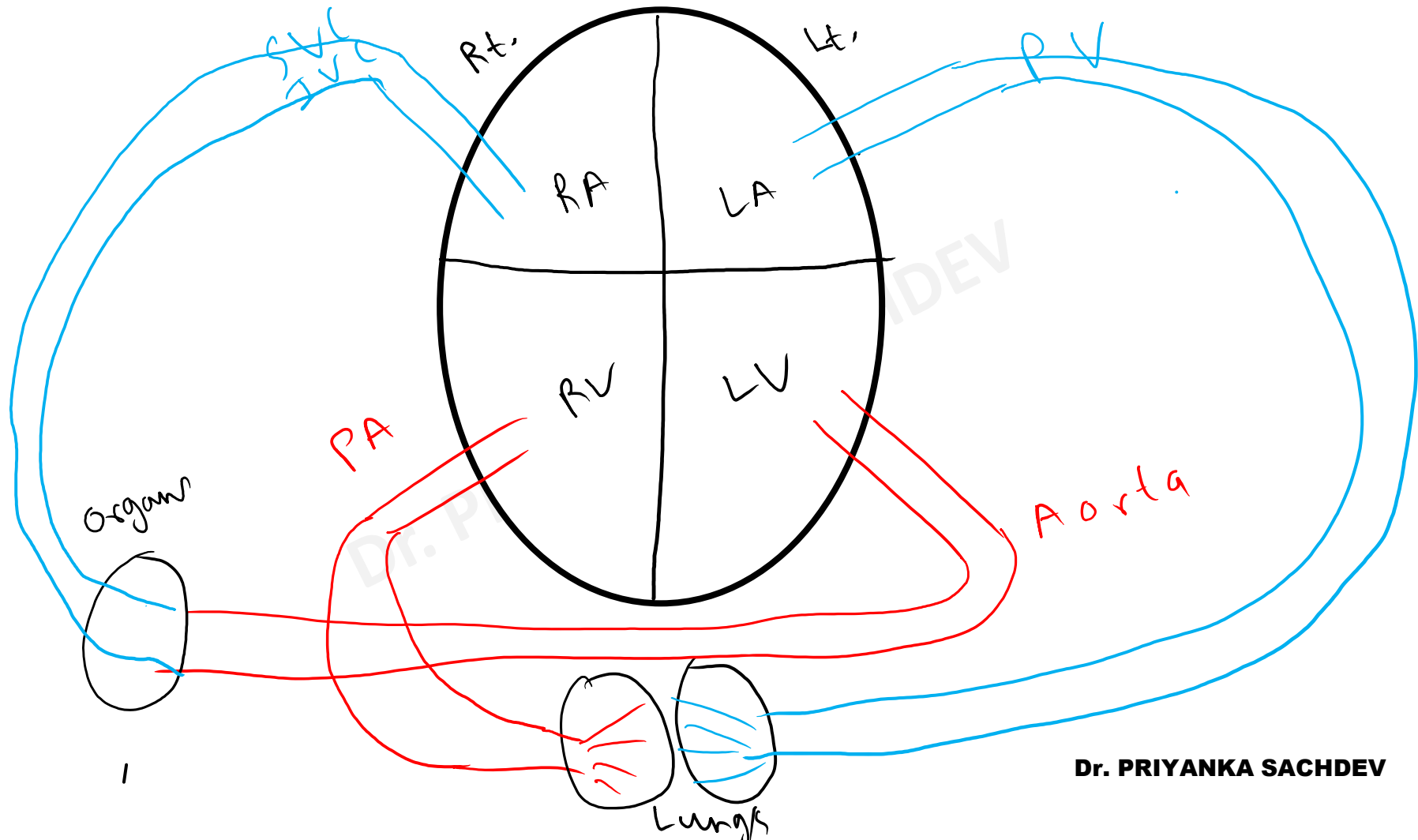


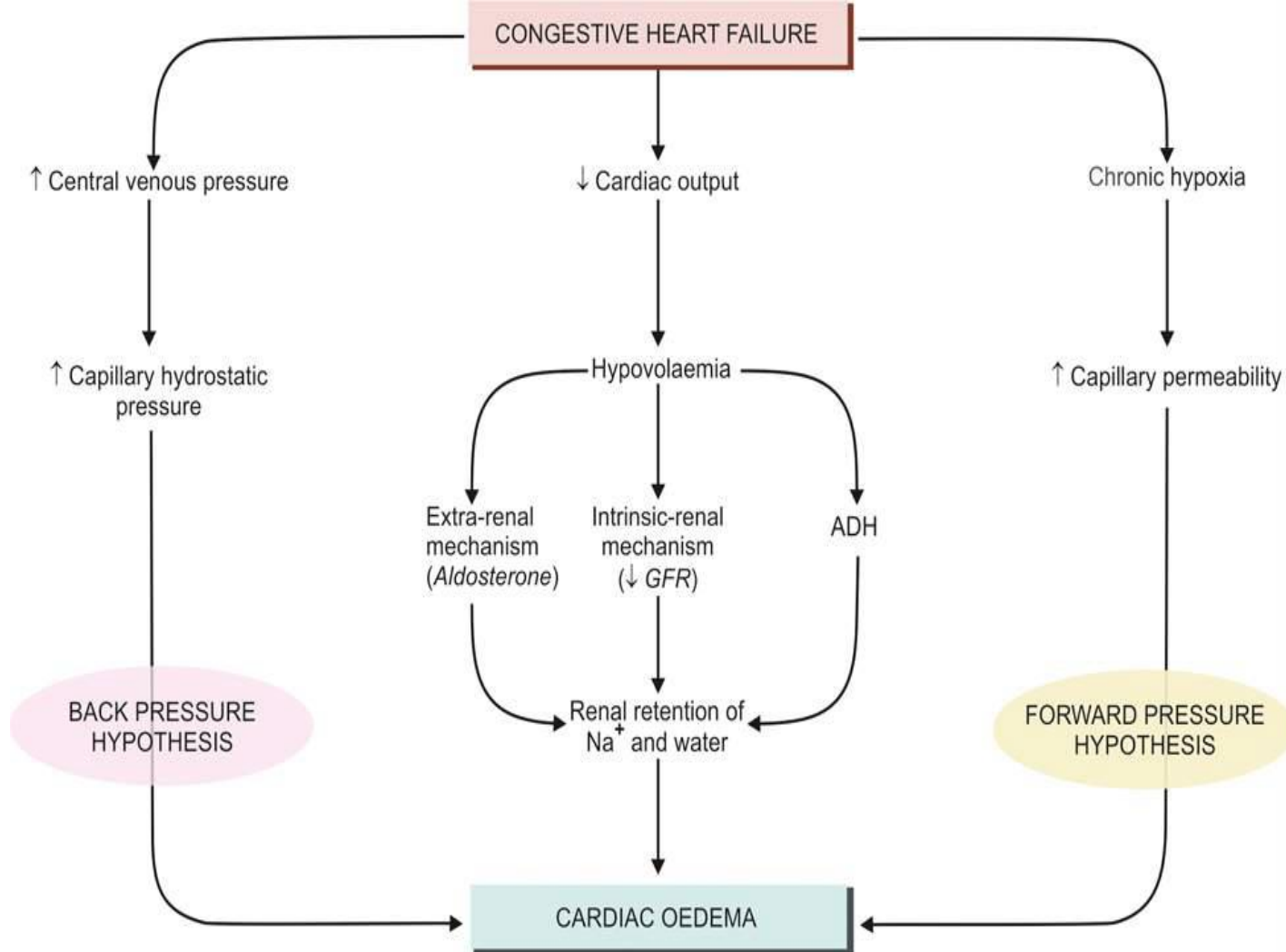
**Increased capillary permeability**



Oedema

However, this theory lacks support since the oedema by this mechanism is exudate whereas the cardiac oedema is typically transudate.





- Cardiac oedema is influenced by gravity and is thus characteristically **dependent oedema** i.e.

- In an **ambulatory patient** it is on **the lower extremities**
- In a **bed-ridden patient** oedema appears on **the sacral and genital areas.**



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# Cardiac Oedema

- **Generalised oedema** develops in **congestive cardiac failure.**
- **Pulmonary oedema** develops in **left-sided cardiac failure.**



# **Left sided heart failure**

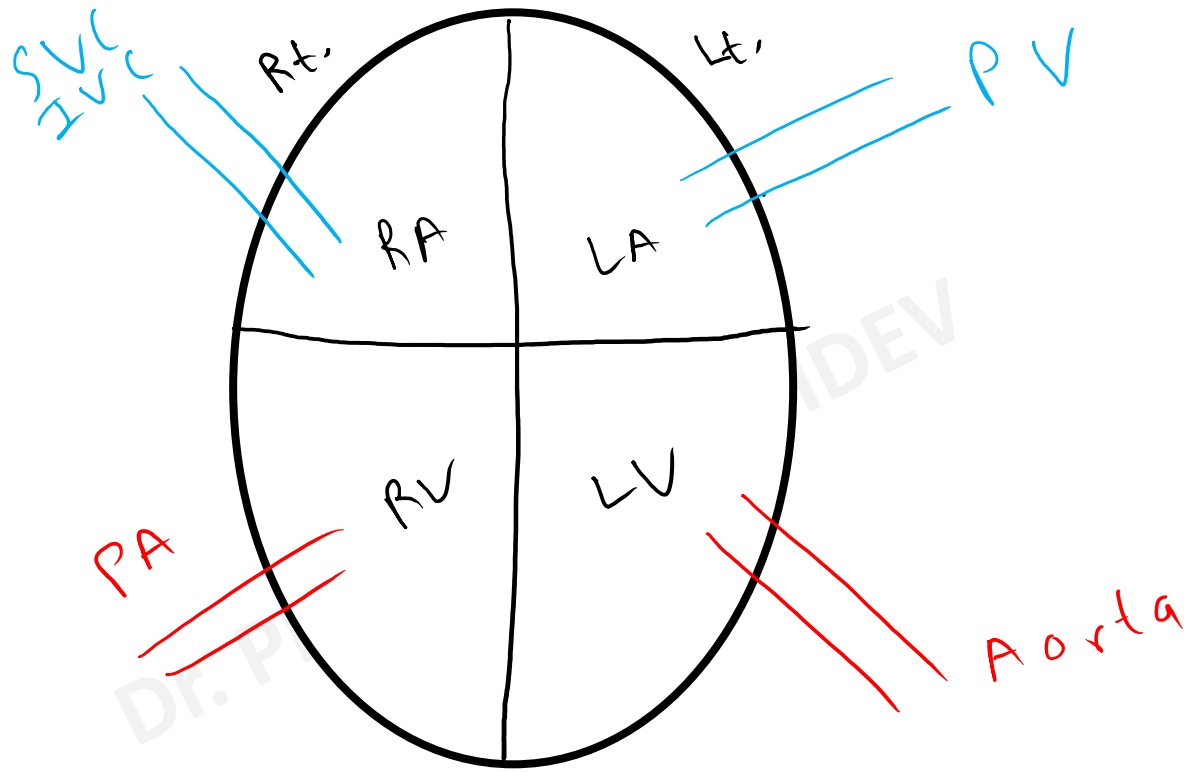
**In left heart failure**

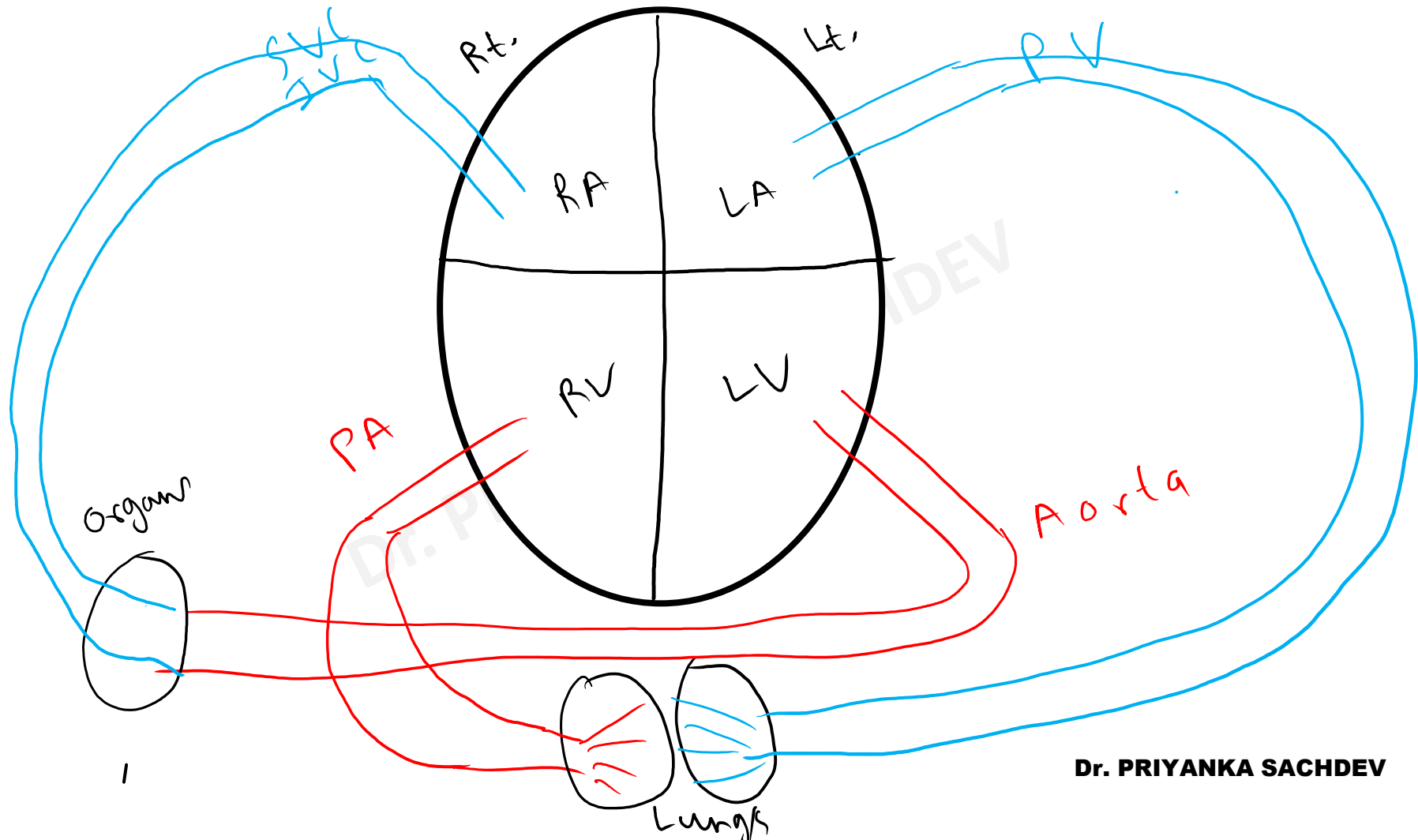


**There is venous congestion, particularly in the lungs**



**Pulmonary oedema rather than generalized oedema**





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# Pulmonary Oedema

- Differs from oedema elsewhere in that the **fluid accumulation is not only in the tissue space but also in the pulmonary alveoli**

**Left heart failure**



**there is increase in the pressure in pulmonary veins**



**transmitted to pulmonary capillaries**



**Increase in pulmonary hydrostatic pressure**



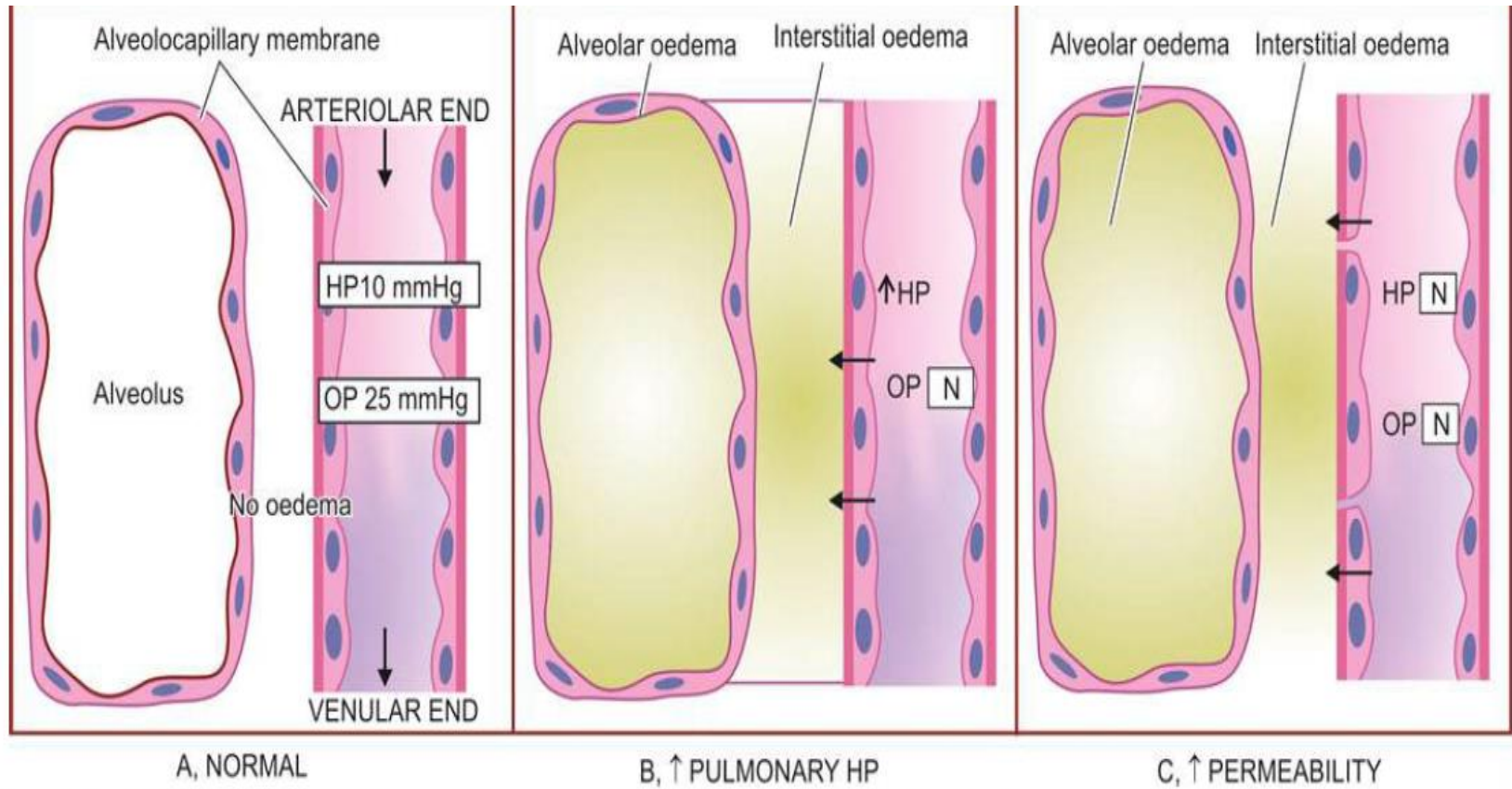
**excessive fluid moves out of pulmonary capillaries into the interstitium of the lungs**



**Interstitial oedema**



**No significant impairment of gaseous exchange**



**Due to high pressure of interstitial oedema**



**The alveolar lining cells break**



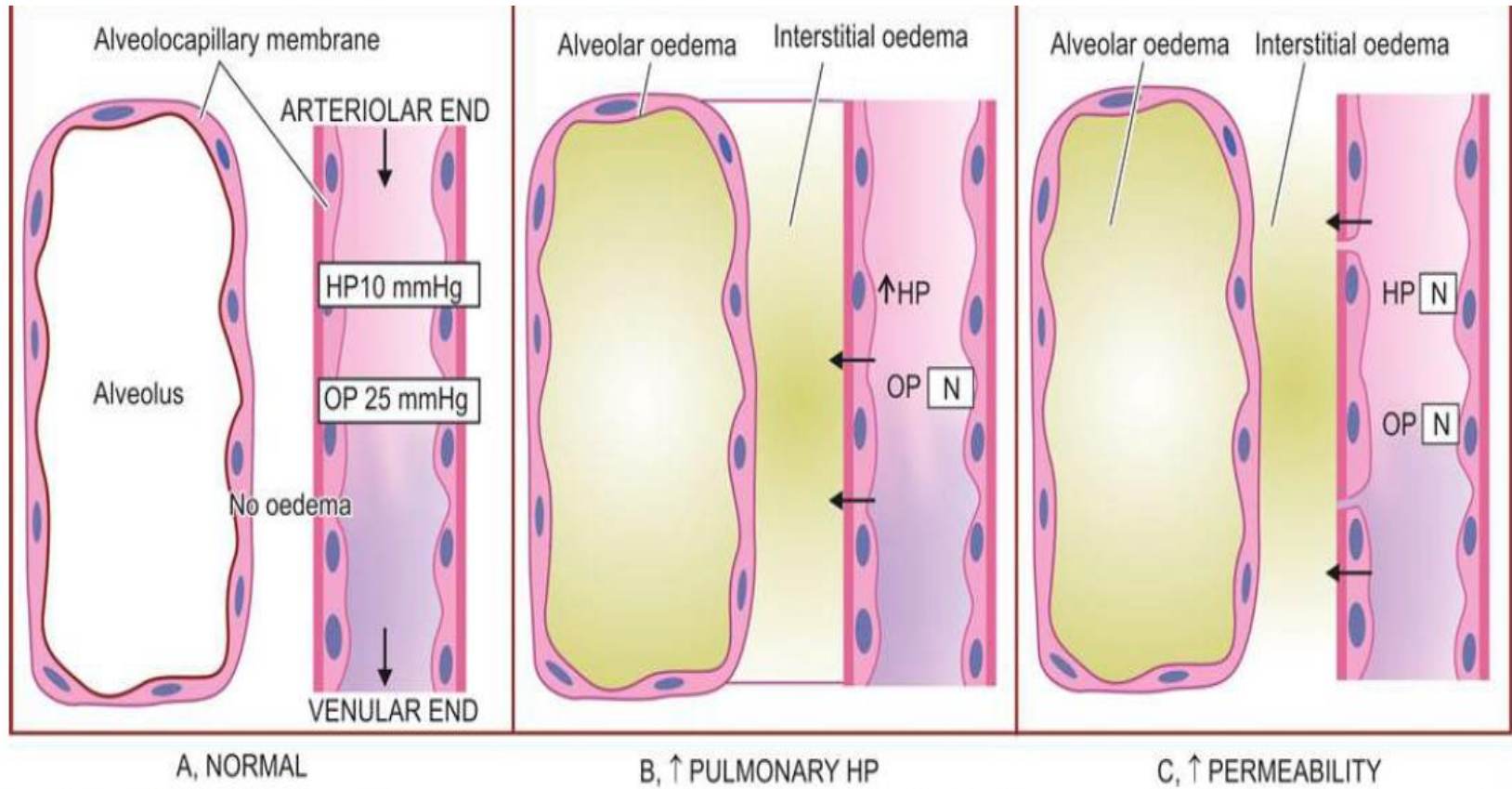
**alveolar air spaces are filled with fluid**



**Alveolar oedema**



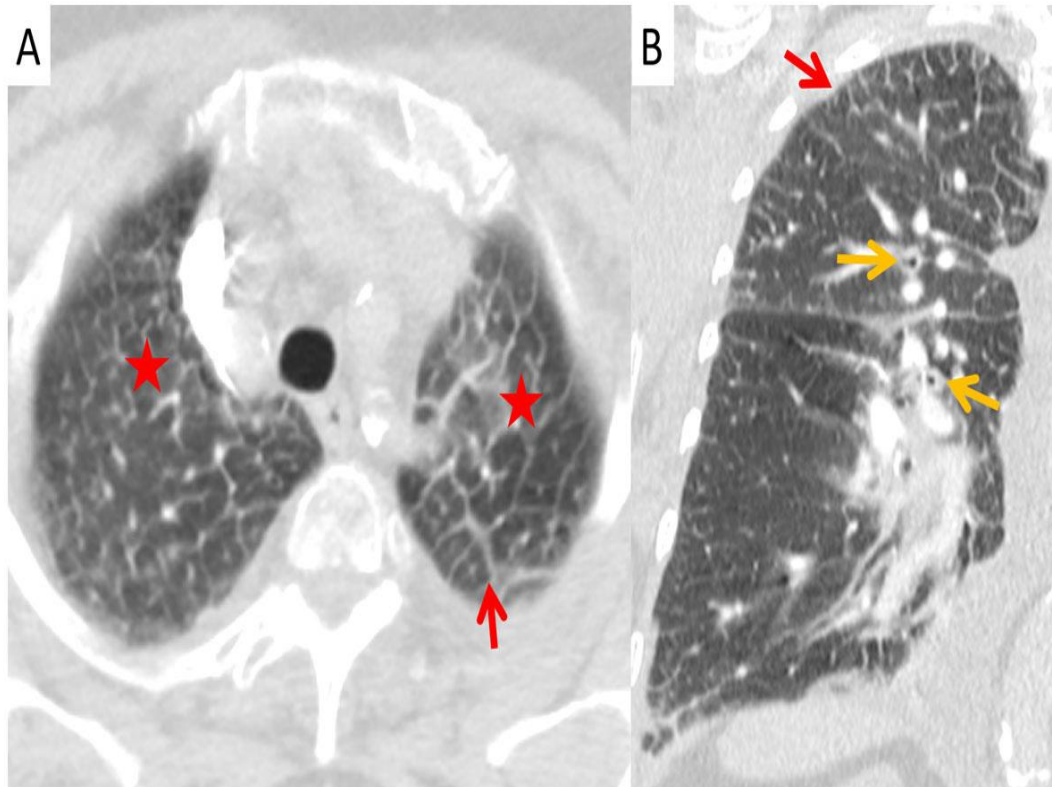
**Driving the air out of alveoli, thus seriously hampering the lung function**





# MORPHOLOGIC FEATURES

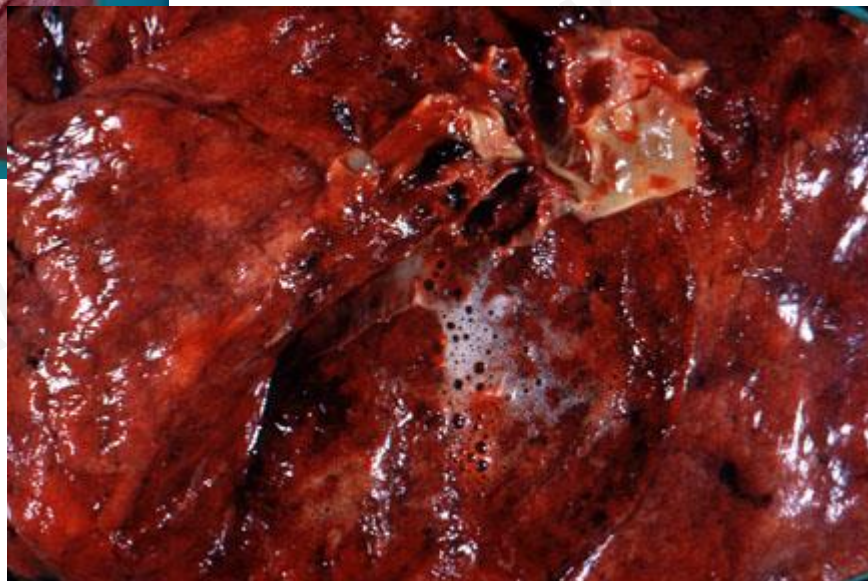
- The fluid accumulates more in the basal regions of lungs.
- The thickened interlobular septa along with their dilated lymphatics may be seen in chest X-ray as linear lines perpendicular to the pleura and are known as **Kerley's lines**



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# Grossly

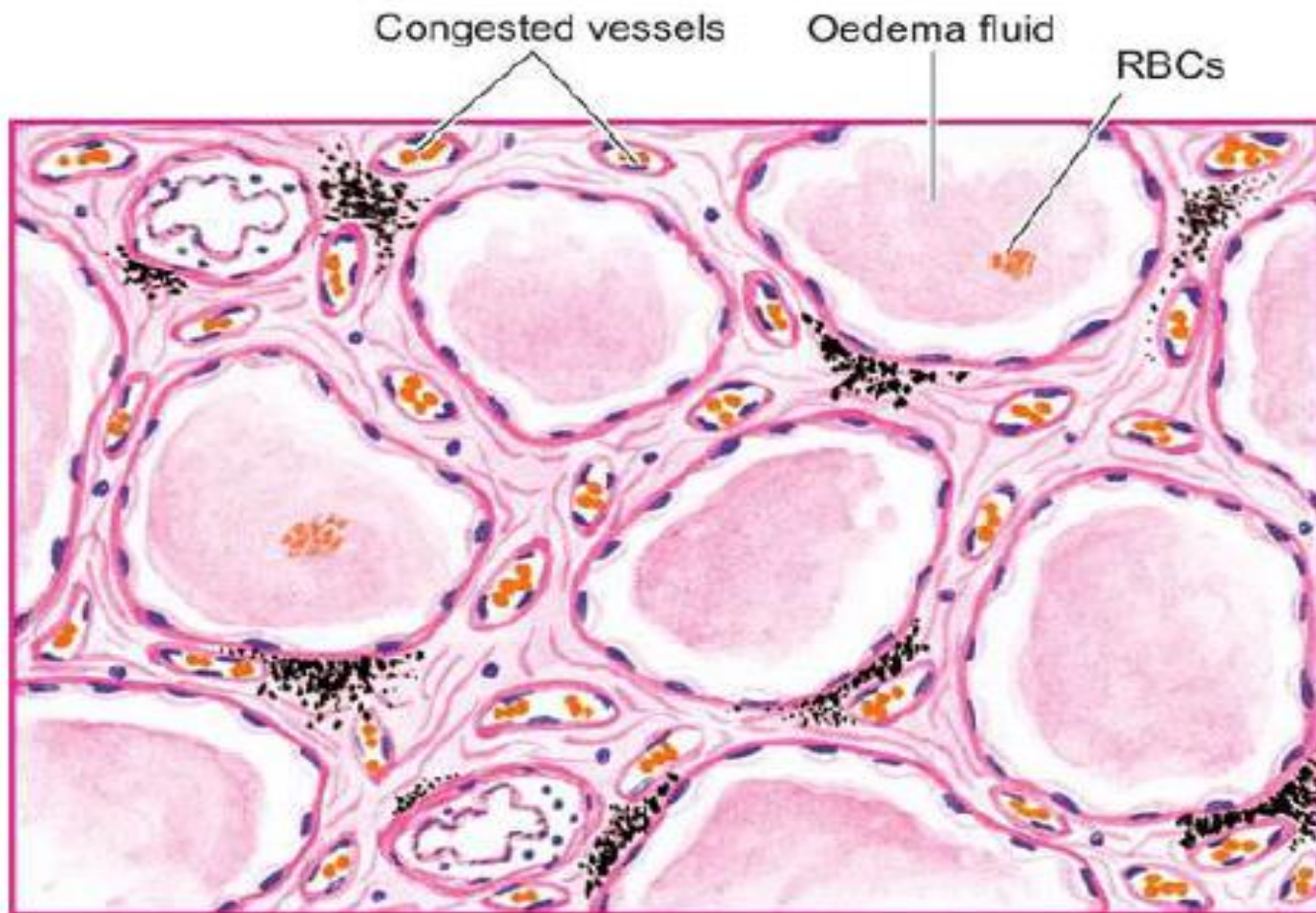
- The lungs in pulmonary oedema are **heavy, moist and subcrepitant.**
- Cut surface exudes **frothy fluid (mixture of air and fluid)**



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# Microscopically

- The alveolar capillaries are congested.
- Initially, the excess fluid collects in the interstitial lung spaces in the septal walls (**interstitial oedema**).
- Later, the fluid fills the alveolar spaces (**alveolar oedema**).
- Oedema fluid in the interstitium as well as the alveolar spaces appears as eosinophilic, granular and pink proteinaceous material, often admixed with some RBCs and alveolar macrophages, also called **heart failure cells**



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# **IMPORTANT TYPES OF OEDEMA**

- **Renal Oedema**
- **Cardiac Oedema**
- **Pulmonary Oedema**
- **Myxoedema**
- **Hepatic Oedema**

# Myxoedema

- Occurs from **hypothyroidism**
- Due to **excessive deposition of glycosaminoglycans (GAGS) in the interstitium.**
- Non-pitting oedema
- On skin of face and other parts of the body as also in the internal organs





Dr.

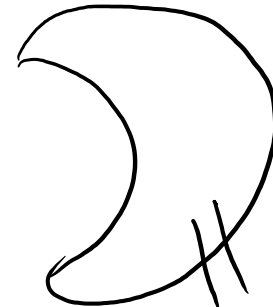
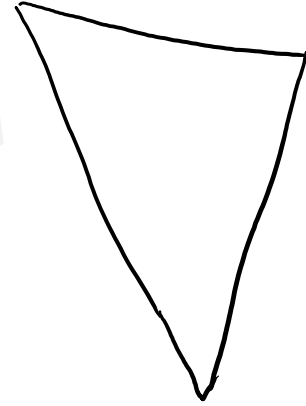
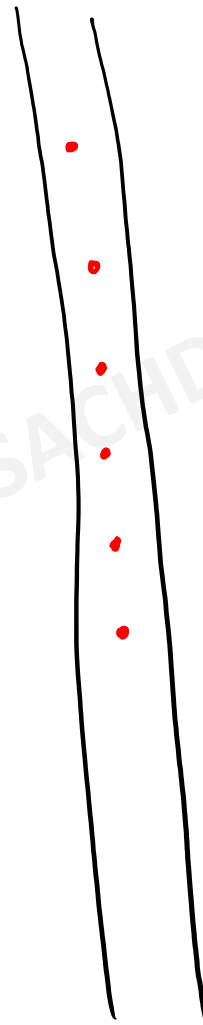
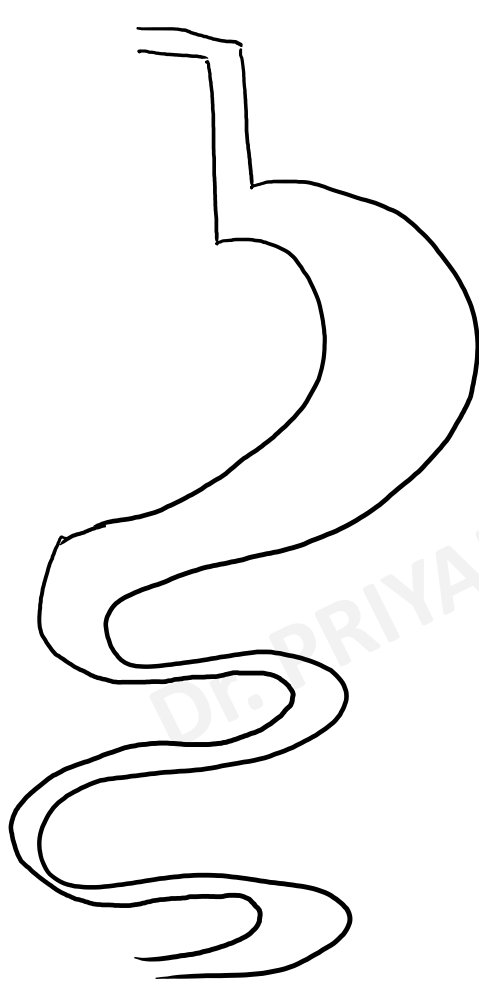
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# **IMPORTANT TYPES OF OEDEMA**

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# Hepatic Oedema

- i) There is **hypoproteinaemia** due to impaired synthesis of proteins by the diseased liver.
- ii) Due to portal hypertension, there is increased venous pressure in the abdomen, and hence **raised hydrostatic pressure**
- iii) Failure of inactivation of aldosterone in the diseased liver and hence hyperaldosteronism → Secondary stimulation of renin-angiotensin mechanism → **sodium and water retention**



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follow us



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# POLLS 1 ????

*Scan or Click to watch  
Cell Adaptation & Injury*



*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*



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**Inceased accumulation of fluid in the interstitial space is described as -**

- a) Edema
- b) Effusion
- c) Transudate
- d) Exudate

Dr. PRIYANKA

**A**

Dr. PRIYANKA SACHDEV



**Odema occurs when plasma protein level is below-**

- a) 8 mg/dl
- b) 2 mg/dl
- c) 5 mg/dl
- d) 10 mg/dl

Dr. PRIYANKA

**C**

Dr. PRIYANKA SACHDEV

**Oedema is caused by fall in plasma proteins below -**

- a) 0.5%
- b) 5%
- c) 15%
- d) 50%

Dr. PRIYANKA

**D**

Dr. PRIYANKA SACHDEV

**Edema is due to-**

- a) Increased capillary osmotic pressure
- b) Decreased hydrostatic pressure in capillaries
- c) Both of the above
- d) Decreased lymph flow

Dr. PK

**D**

Dr. PRIYANKA SACHDEV

**All of the following are included in pathogenesis of edema except?**

- a) Decreased hydrostatic pressure of capillaries
- b) Decreased plasma osmotic pressure of capillaries
- c) Lymphatic obstruction
- d) Increased vascular permeability

Dr. PRIYANKA

**A**

Dr. PRIYANKA SACHDEV



**The definition of exudate is -**

- a) Extravascular fluid that has a high protein concentration and contains cellular debris
- b) Extravascular fluid that has a low protein concentration
- c) Extravascular fluid with high glucose concentration
- d) Extravascular fluid with low glucose concentration

**A**

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Edema in nephrotic syndrome occurs due to

- (a)  $\text{Na}^+$  and water restriction
- (b) Increased venous pressure
- (c) Decreased serum albumin
- (d) Decreased fibrinogen

Dr. PRIYANKA

**C**

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A 54-year-old chronic alcoholic Adhiya Kumar is brought by his son as he has developed progressively increasing abdominal distension from past 3 months. The physician aspirates the abdominal fluid which is straw-colored and clear and is found to have protein content (mainly albumin) of 2.3 g/dl. Which of the following is a major contributor to the fluid accumulation in this patient?

- (a) Blockage of lymphatics
- (b) Decreased oncotic pressure
- (c) Decreased capillary permeability
- (d) Inflammatory exudation

# B

- The patient in the stem of the question is most likely having liver cirrhosis secondary to chronic alcoholism.
- An important manifestation of this disease is reduced hepatic synthesis of albumin which is the most important contributor to plasma oncotic pressure.
- Also, ascites is associated with increased sodium and water retention because of stimulation of the reninangiotensin aldosterone system (RAAS).

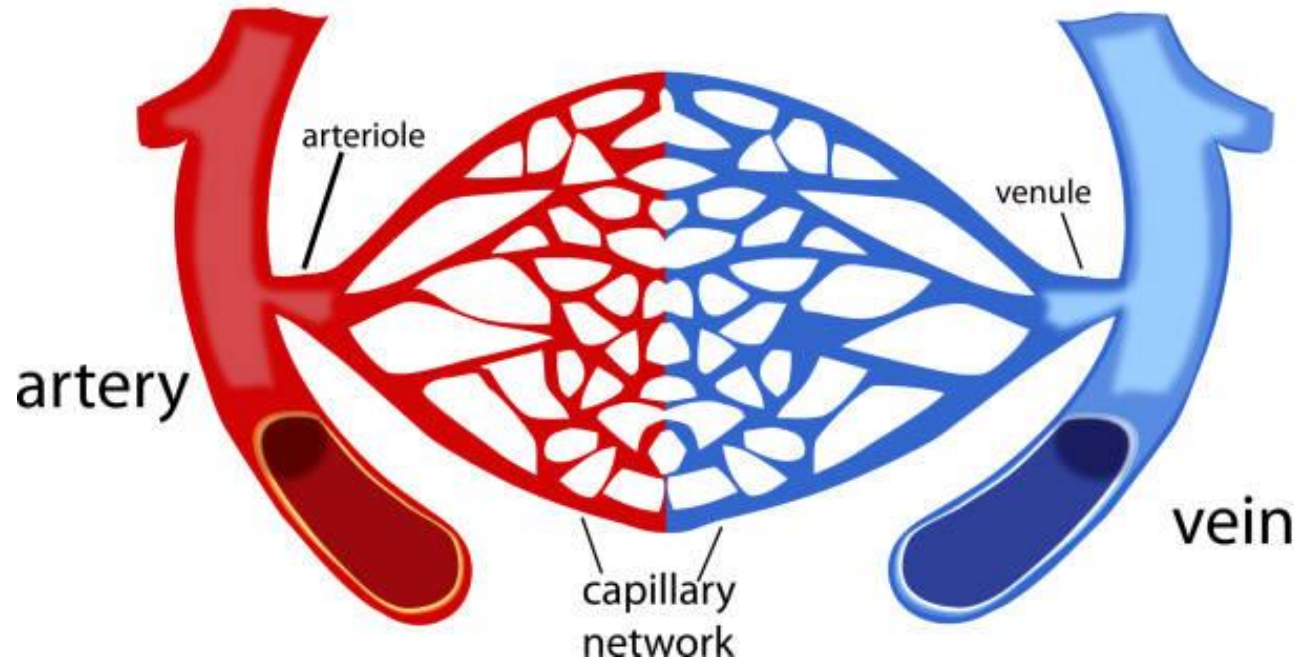
- **Oedema**
- **Hyperamia and congestion**
- **Thrombosis**
- **Embolism**
- **Ischemia**
- **Infaction**
- **Shock**

# **HYPERAEMIA AND CONGESTION**

**Localised increase in the volume of blood within dilated vessels of an organ or tissue.**

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# HYPERAMIA

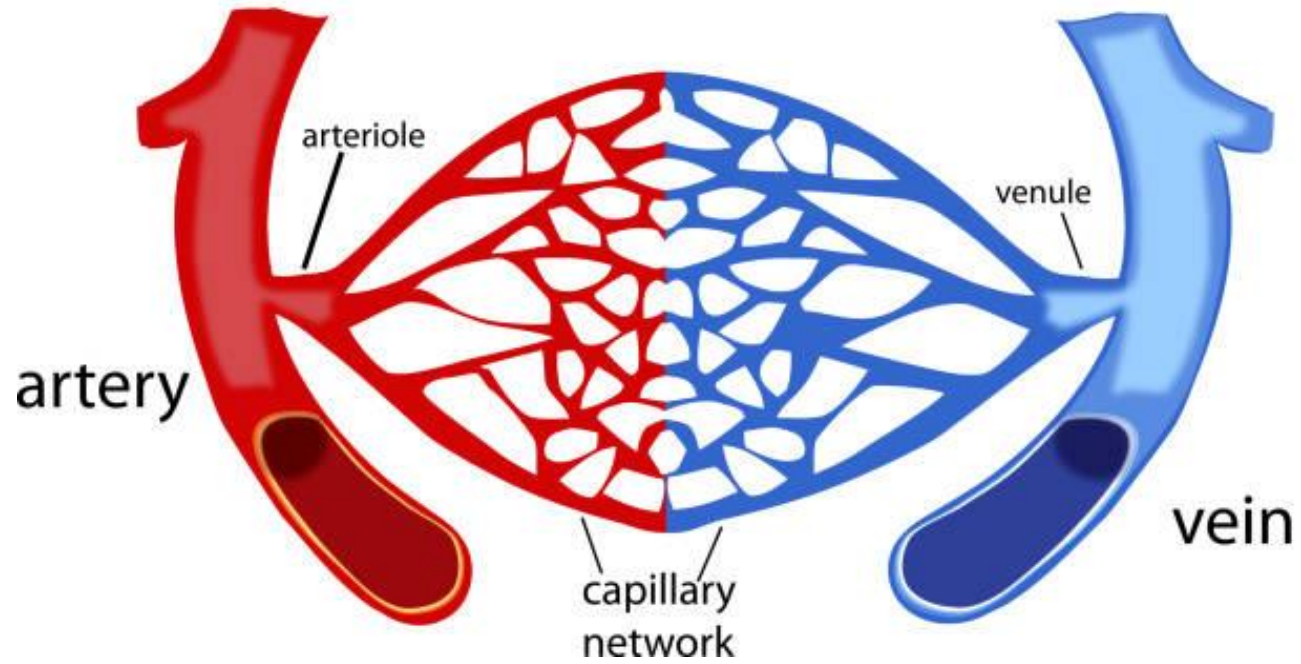
- Increased volume of blood from **arterial dilatation** (i.e. increased inflow) is called **hyperaemia (active hyperamia)**
- It is an **active process**
- Affected tissues turn red (**erythema**) because of increased delivery of oxygenated blood.

# Examples→

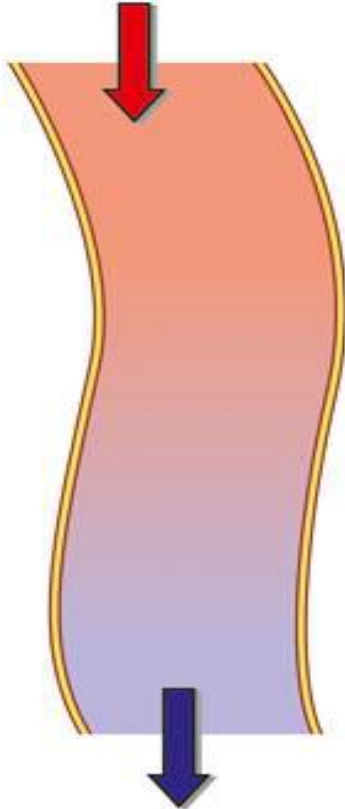
- i) Inflammation e.g. congested vessels in the walls of alveoli in pneumonia
- ii) Blushing i.e. flushing of the skin of face in response to emotions
- iii) Muscular exercise
- iv) High grade fever

# CONGESTION

- Increased volume of blood from **impaired venous drainage** (i.e. diminished outflow) is called **congestion ( passive hyperaemia )**
- It is a **passive process**
- Affected tissues turn blue (**cyanosis**) because of increased delivery of deoxygenated blood.



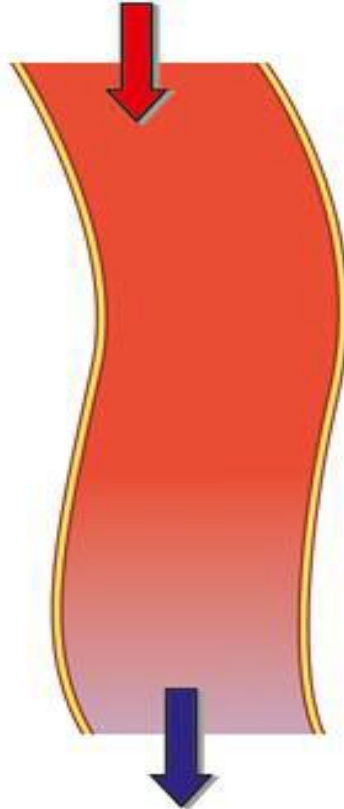
Normal arterial inflow



Normal venous outflow

NORMAL

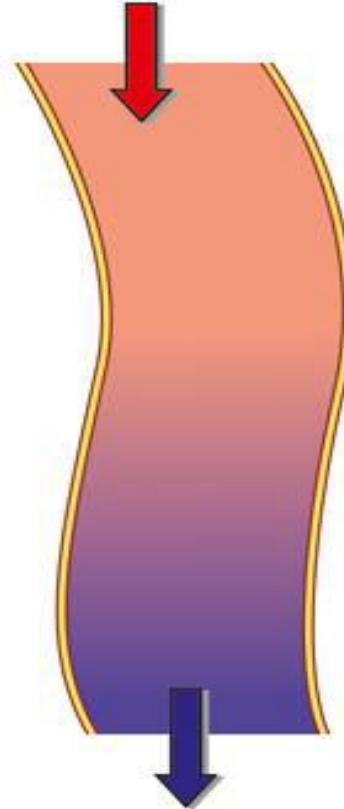
Increased arterial inflow



Normal or increased venous outflow

HYPERAEMIA

Normal arterial inflow



Decreased venous outflow

PASSIVE  
CONGESTION

ACHDEV

# Hyperaemia vs Congestion

**Both = Increased volume of blood in tissue**

## Hyperaemia

- active process
- arteriolar dilation
- Affected organ- pink/Red
- e.g. skeletal muscle during exercise (physiologic), inflammation (pathologic)

## Congestion

- passive process
- impaired venous outflow
- Affected organ- bluish
- e.g. cardiac failure (systemic), venous obstruction (local)
- Local / systemic

# **HYPERMIA AND CONGESTION**

## **Differences:**

	<b>HYPEREMIA</b>	<b>CONGESTION</b>
<b>1</b>	<b>An active process</b>	<b>A passive process</b>
<b>2</b>	<b>Increased blood flow (vasodilatation)</b>	<b>Impaired blood flow</b>
<b>3</b>	<b>During exercise &amp; in inflammation</b>	<b>Venous obstruction &amp; cardiac failure</b>
<b>4</b>	<b>Oxygenated blood (Redder)</b>	<b>Deoxygenated blood (Cyanosed)</b>



# **Congestion**

•2 types→

1.Acute

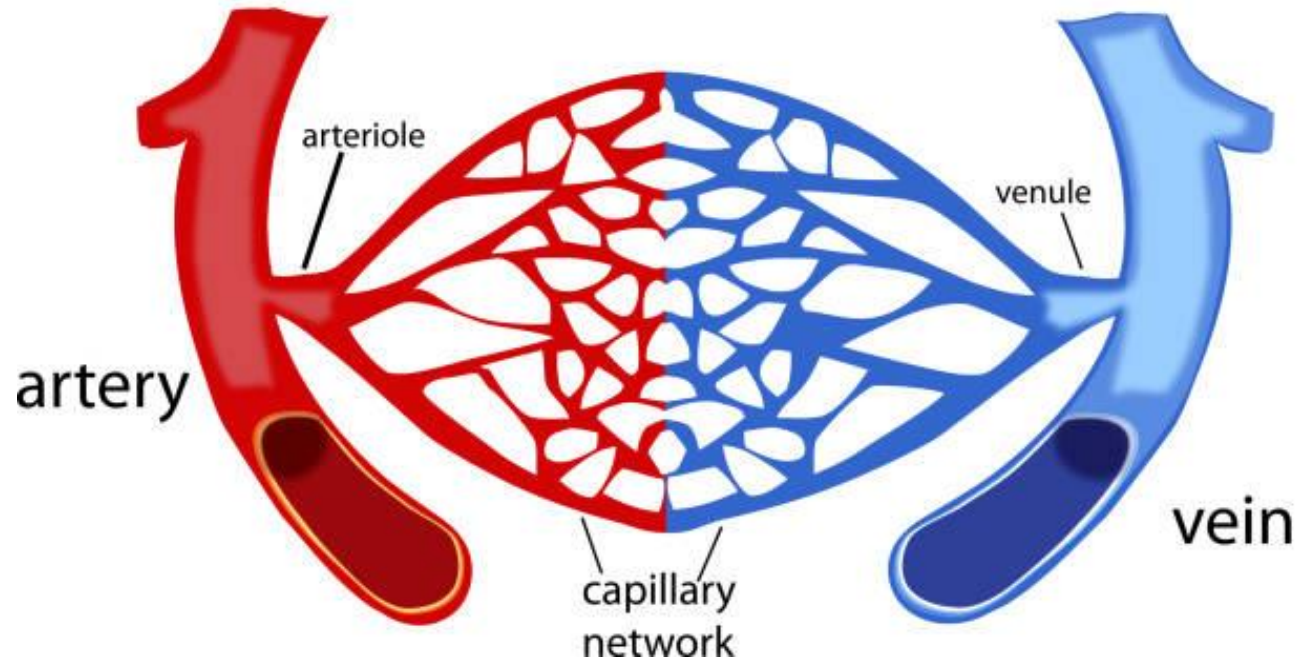
2.Chronic (chronic venous congestion  
(CVC))

## Acute congestion →

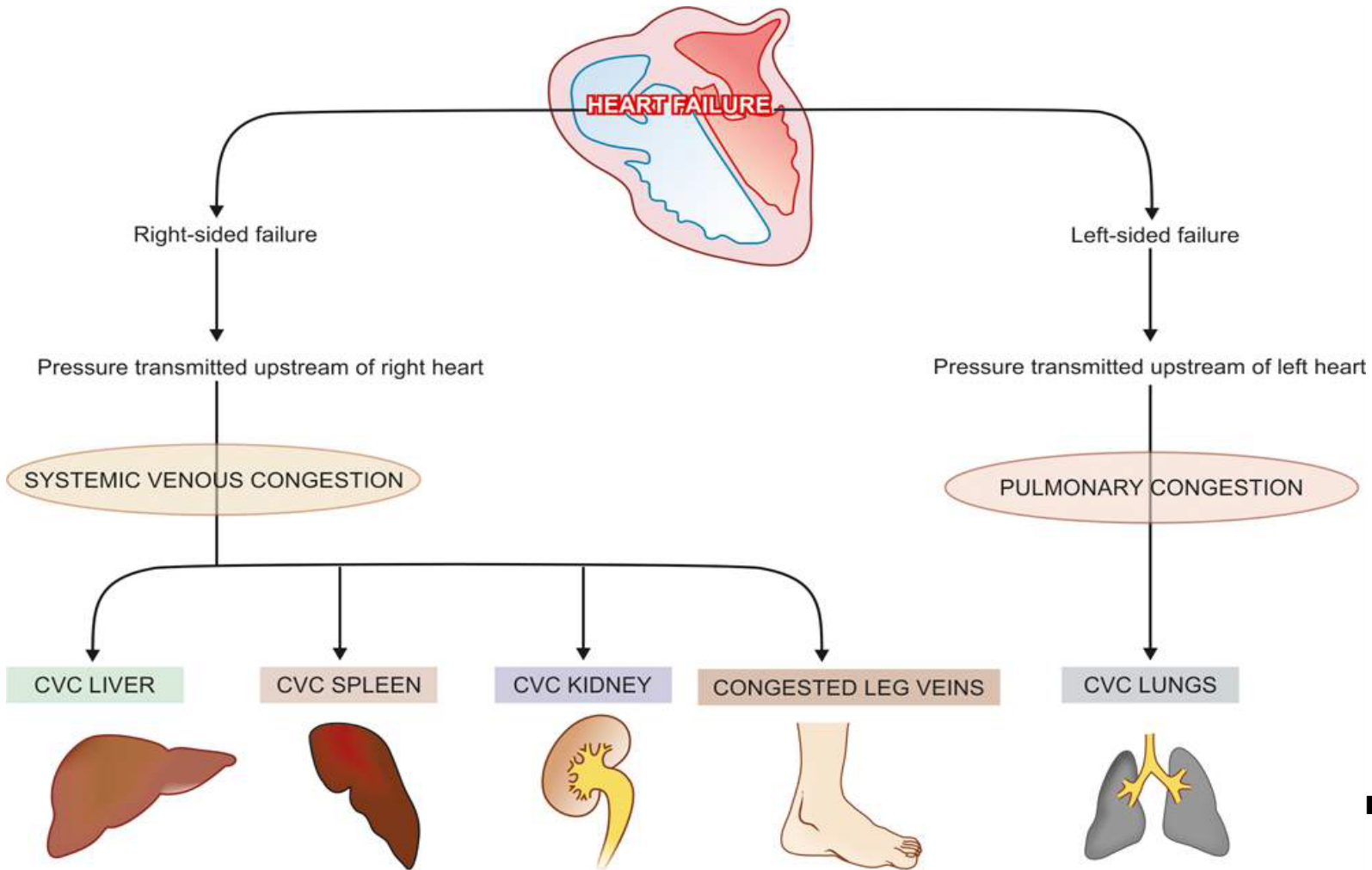
- As a result of increased hydrostatic pressures, congestion commonly leads to **edema**.

## Chronic venous congestion (CVC) →

- the associated chronic hypoxia may result in **ischemic tissue injury and scarring**.
- In chronically congested tissues, capillary rupture can also produce small **hemorrhagic foci**; subsequent catabolism of extravasated RBCs by macrophages.



- **In left-sided heart failure** → pulmonary congestion (or **CVC lungs**) results
- **In right-sided heart failure** → systemic venous congestion (i.e. **CVC of systemic organs** → **Liver, spleen** ) results



- CVC Lung
- CVC Liver
- CVC Spleen

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# CVC Lung

Grossly→

- The lungs are heavy and firm in consistency
- Cut surface is dark and rusty brown in colour→ **brown induration of the lungs.**

***Chronic venous congestion of the lung - Gross***





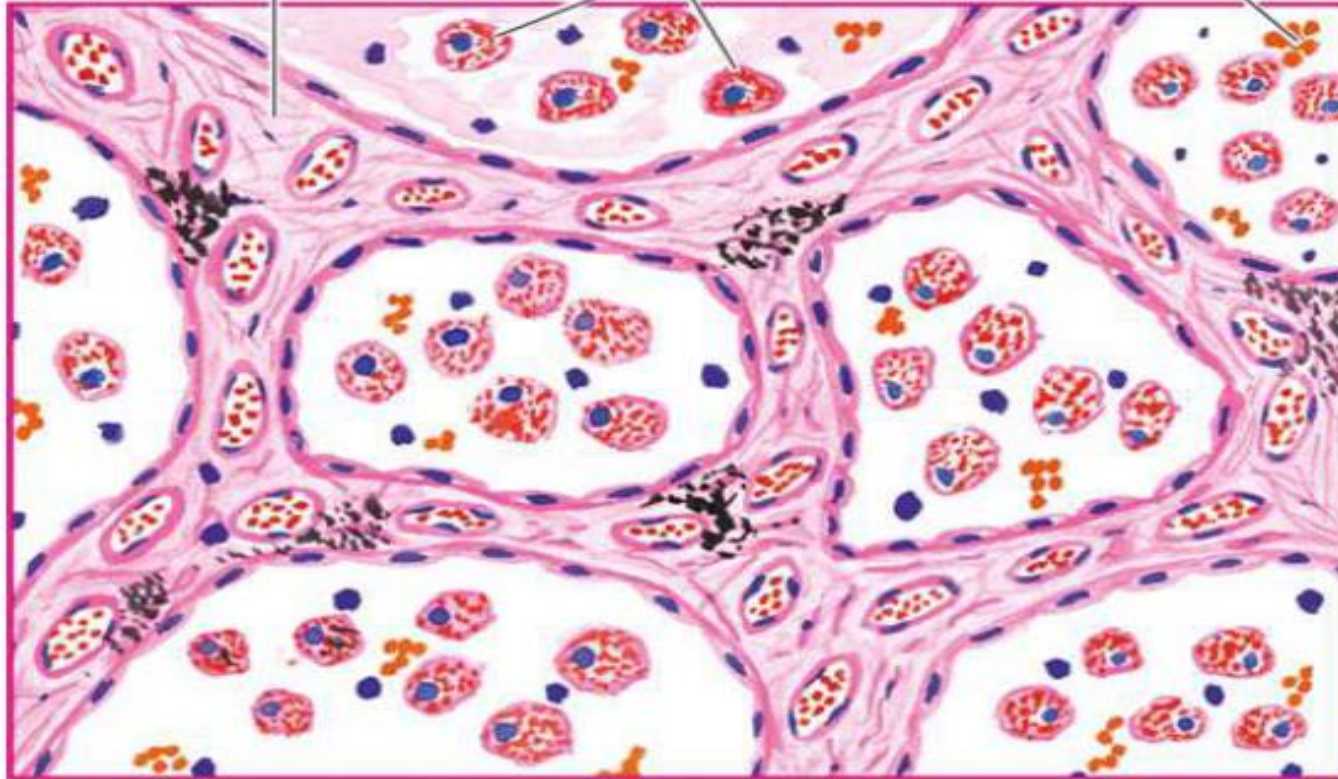
# Microscopically

- i) The alveolar septa are widened due to presence of **interstitial oedema**
- ii) Rupture of dilated and congested capillaries may result in minute intra-alveolar haemorrhages.
- iii) The breakdown of RBC liberates haemosiderin pigment which is taken up by alveolar macrophages, called as **heart failure cells** (brown induration)

Thickened alveolar septa

Heart failure cells

Intra-alveolar RBCs



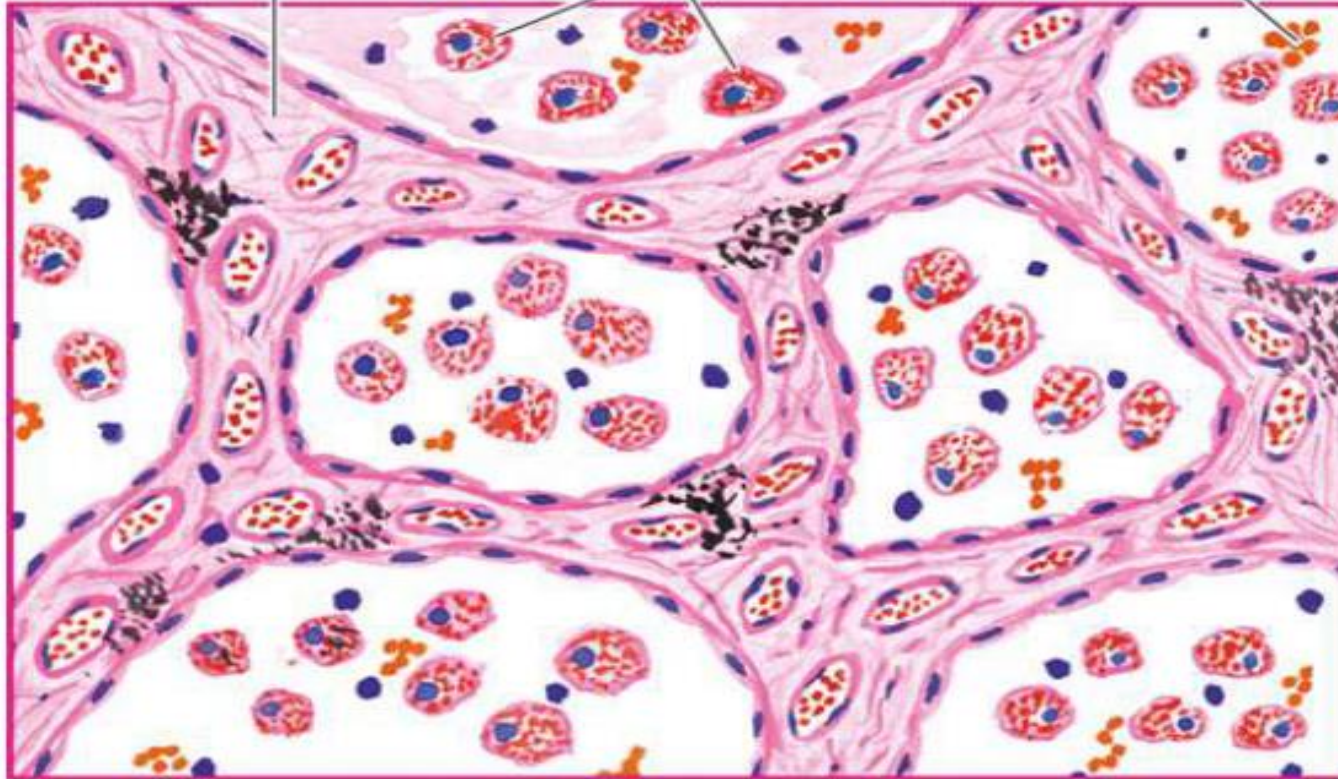
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- Heart failure cells are present in the lungs and **NOT** in the heart.
- These are hemosiderin laden macrophages.

Thickened alveolar septa

Heart failure cells

Intra-alveolar RBCs



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- CVC Lung
- CVC Liver
- CVC Spleen

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# CVC Liver

## Grossly→

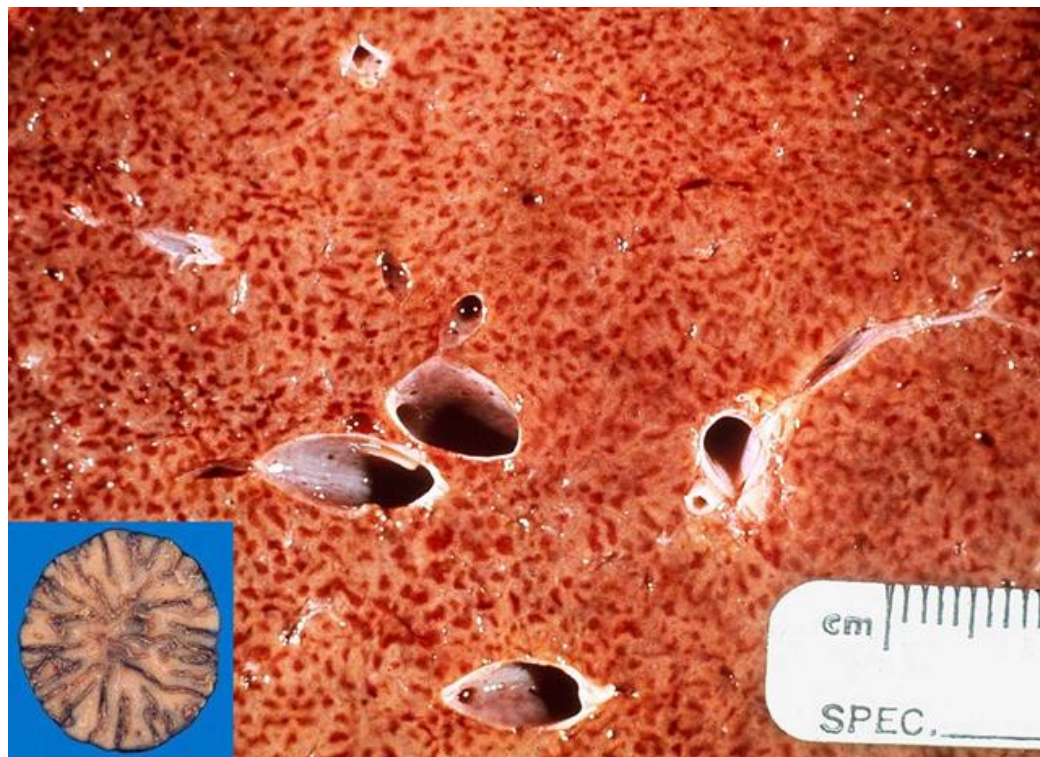
- The liver is enlarged and tender
- Capsule is tense.
- Cut surface shows characteristic **nutmeg appearance** due to red and yellow mottled appearance, corresponding to congested centre of lobules and fatty peripheral zone respectively



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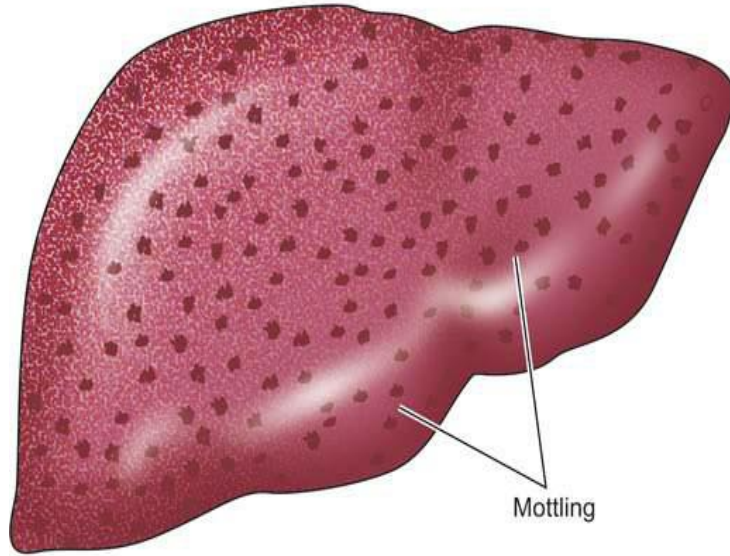
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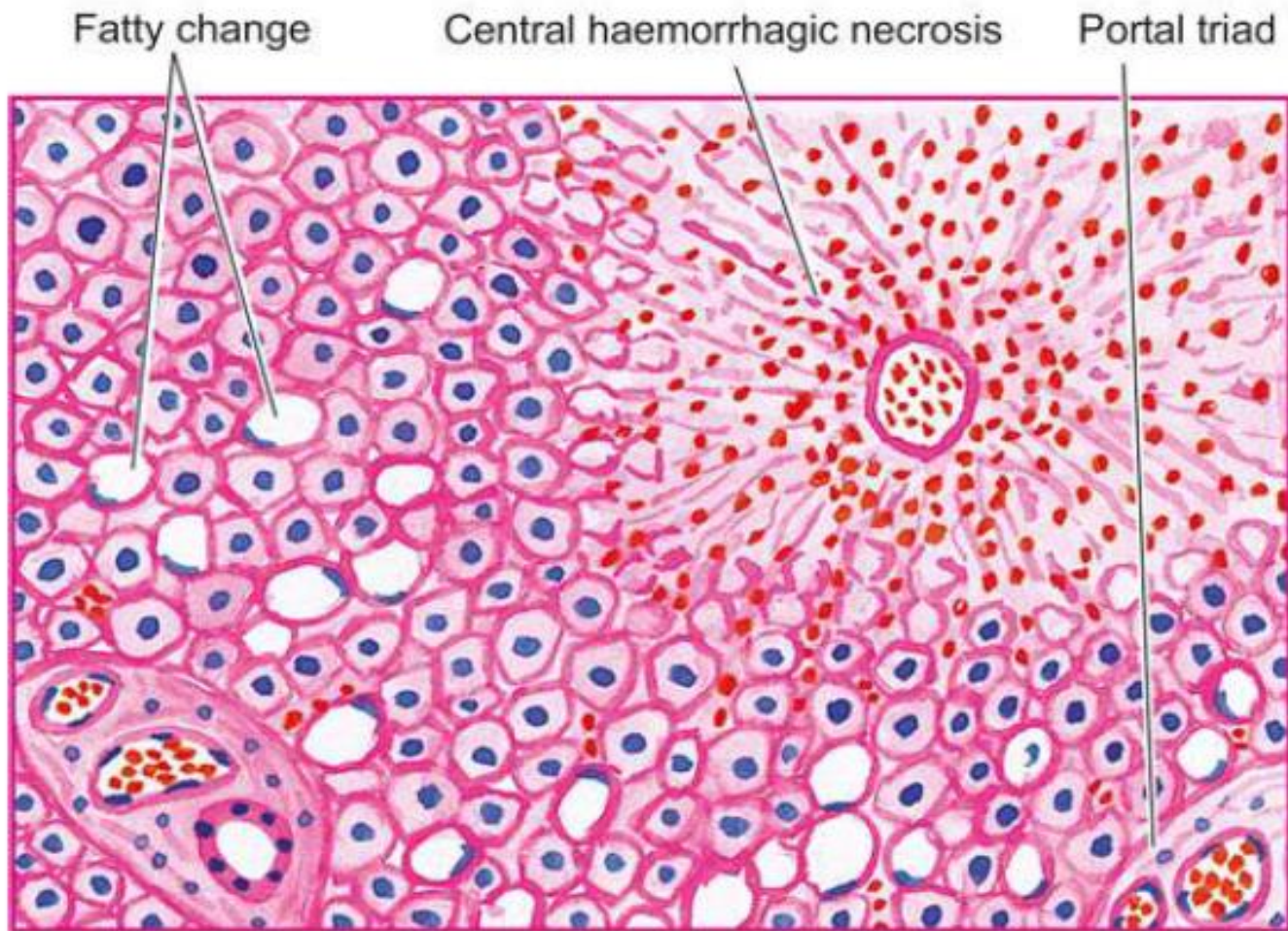




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# Microscopically→

- The central veins is distended and filled with blood.
- The centrilobular hepatocytes undergo degenerative changes and **Centrilobular haemorrhagic necrosis** occurs.
- The peripheral zone of the lobule is less severely affected by chronic hypoxia and shows **fatty change** in the hepatocytes
- So **nutmeg appearance**



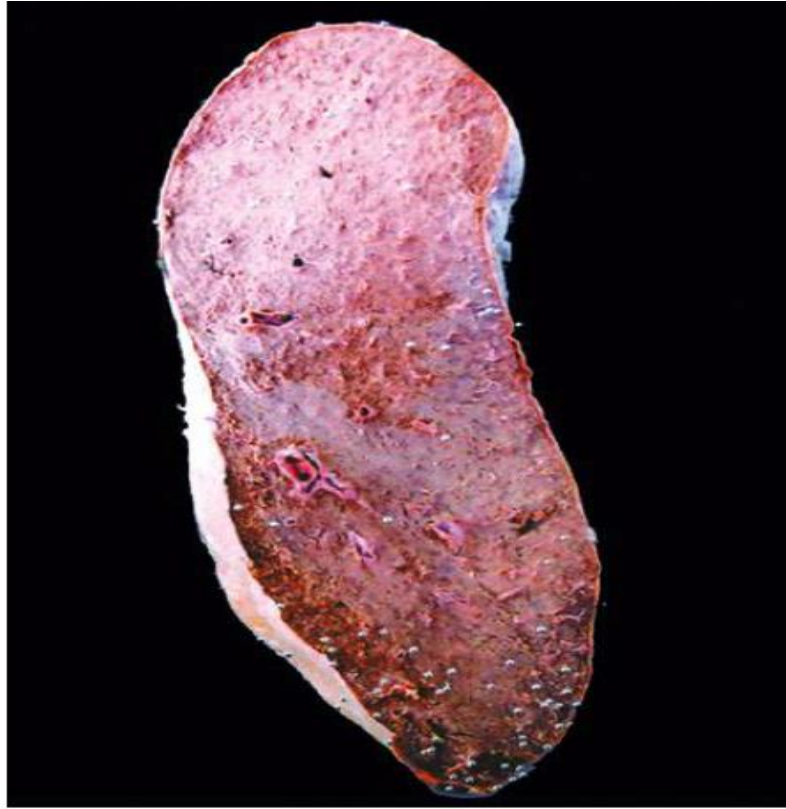
- CVC Lung
- CVC Liver
- CVC Spleen

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# CVC Spleen

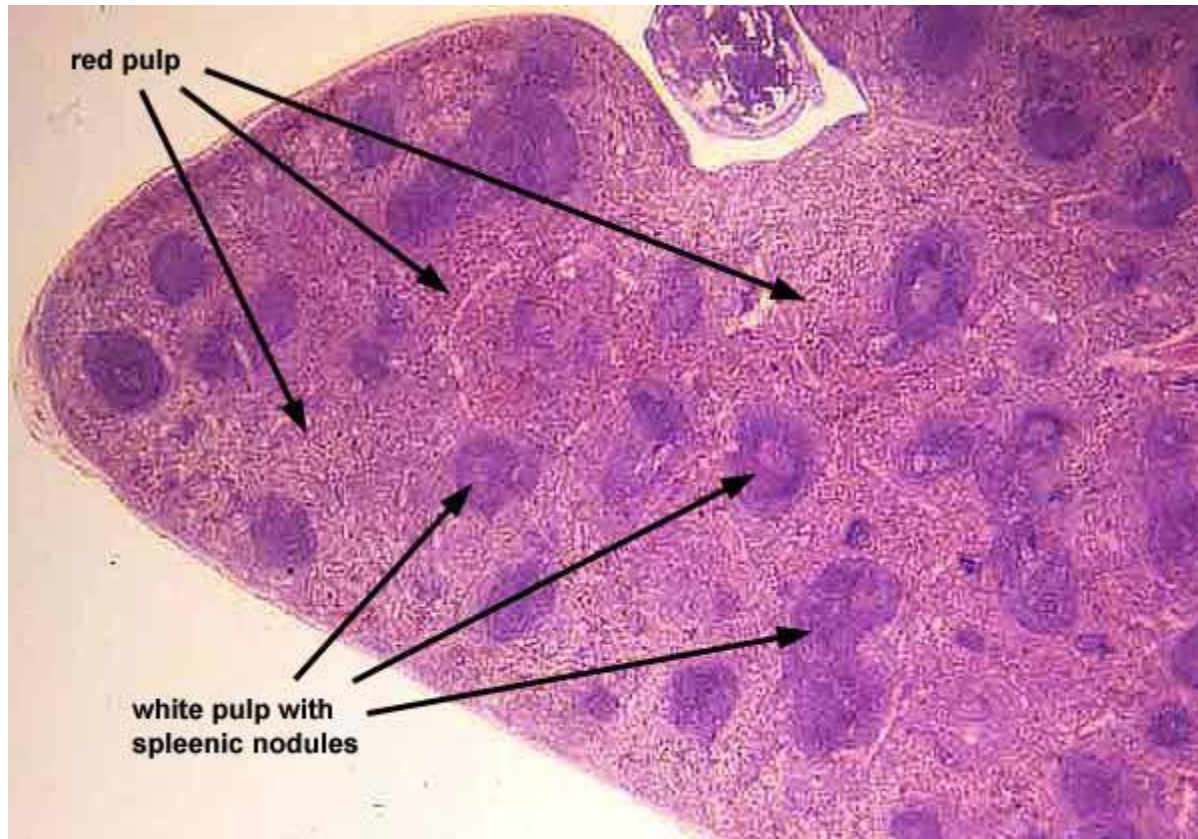
Grossly→

- Enlarged
- The organ is deeply **congested, tense and cyanotic**
- Sectioned surface is **gray tan**



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# Microscopically →

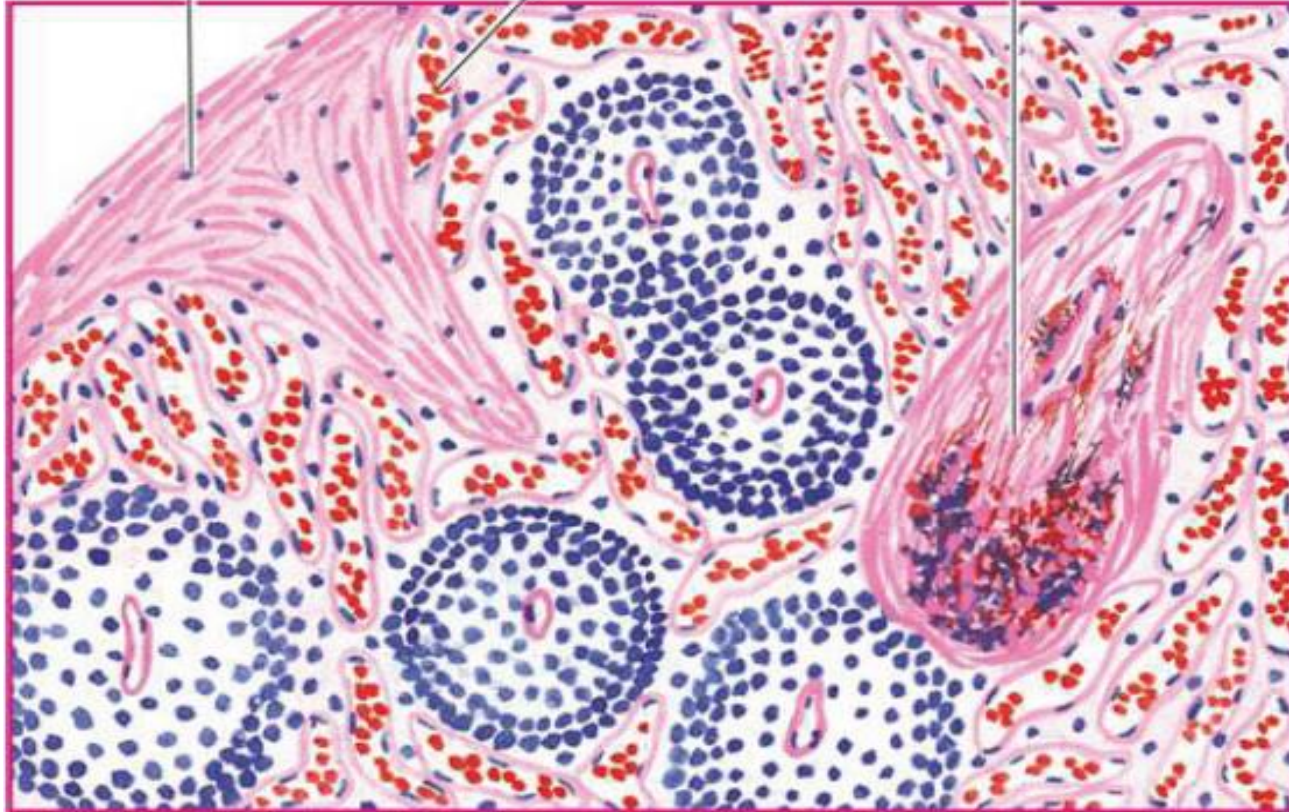
- **Red pulp** is enlarged due to marked sinusoidal dilatation
- There are areas of recent and old haemorrhages.
- Sinusoids may get converted into capillaries (**capillarisation of sinusoids**).
- There is hyperplasia of reticuloendothelial cells in the red pulp of the spleen (splenic macrophages).



Thickened capsule

Congested sinusoids

Gamna-Gandy body

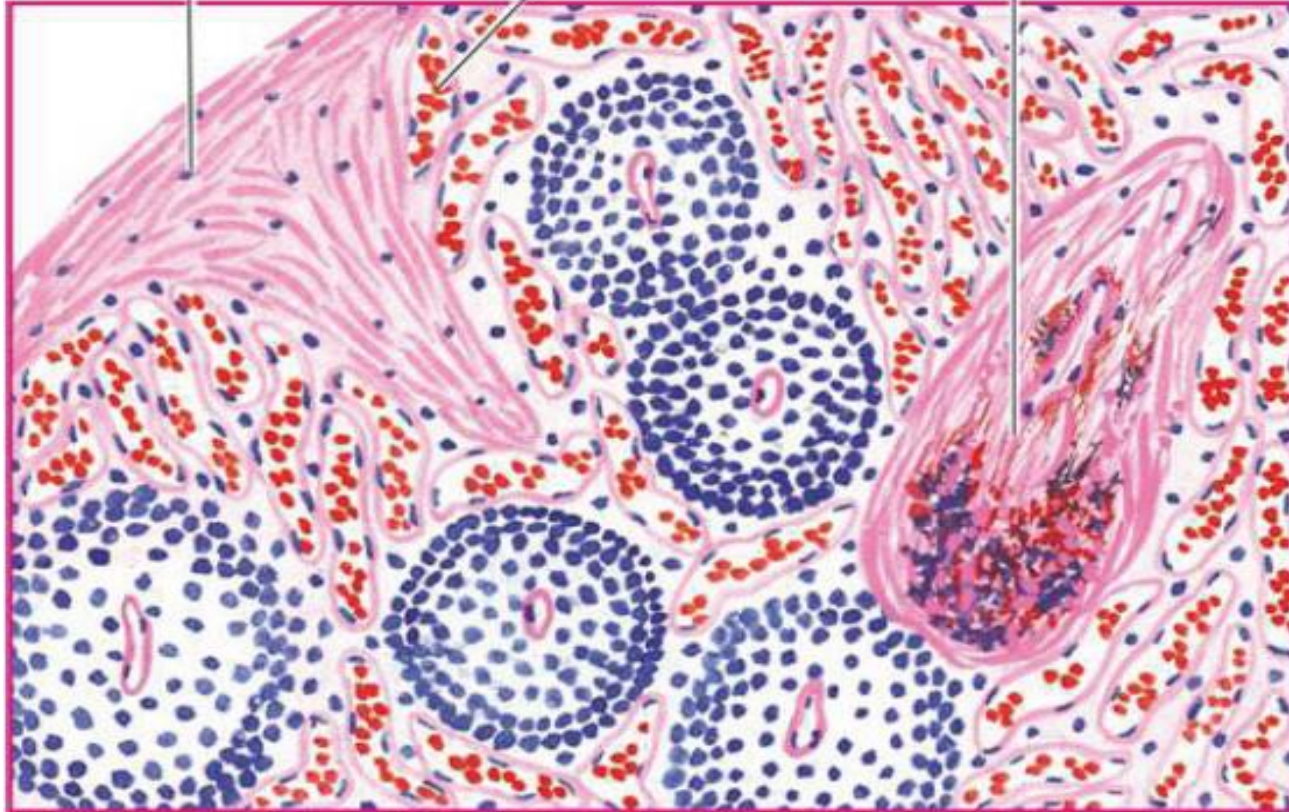


- There is fibrous thickening of the capsule and of the trabeculae.
- Some of haemorrhages overlying fibrous tissue get deposits of haemosiderin pigment → **Gamna-Gandy bodies**

Thickened capsule

Congested sinusoids

Gamna-Gandy body



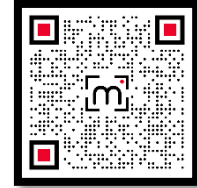
# REMEMBER

- **CVC of lung** is characterized by presence of **heart failure cells** (hemosiderin laden macrophages)
- **CVC of liver** produces **nut-meg liver**
- **CVC of spleen** is characterized by presence of **Gamna-Gandy bodies**

# Revision

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- CVC Lung
- CVC Liver
- CVC Spleen

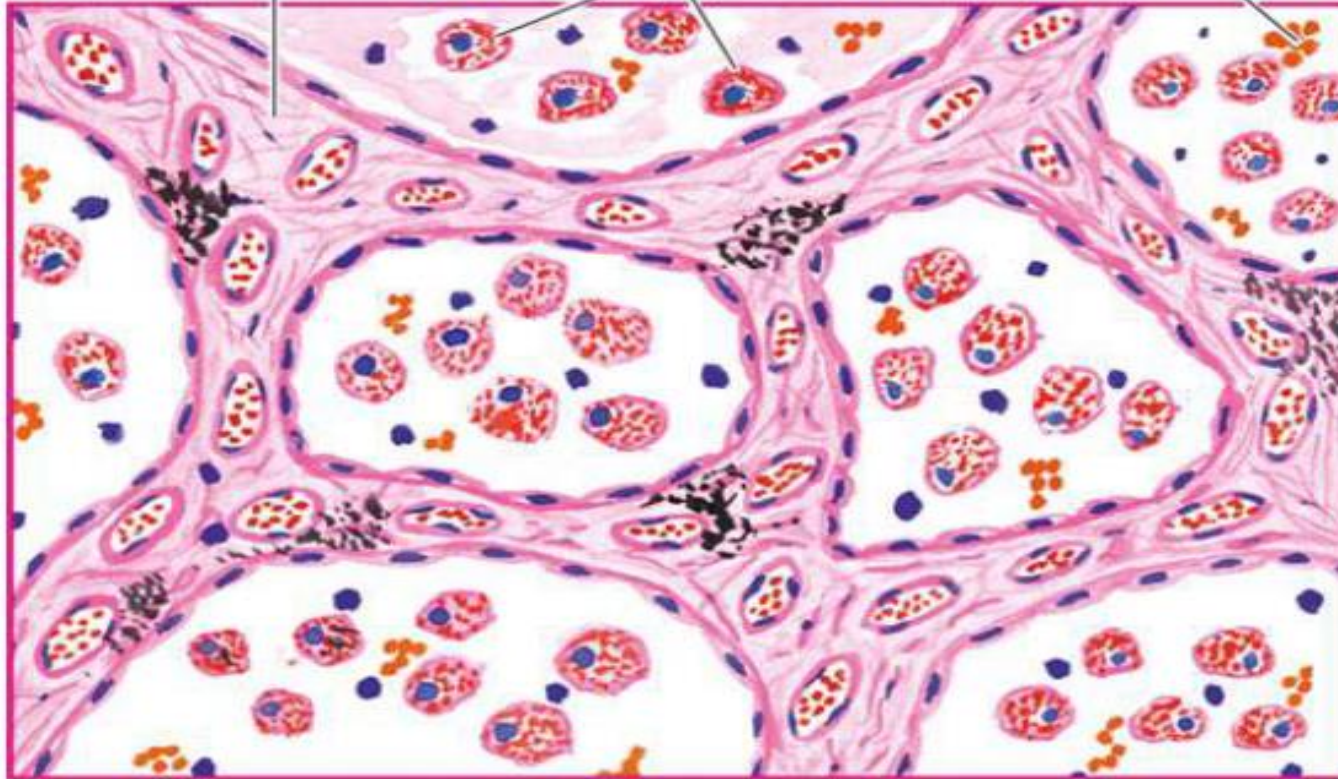
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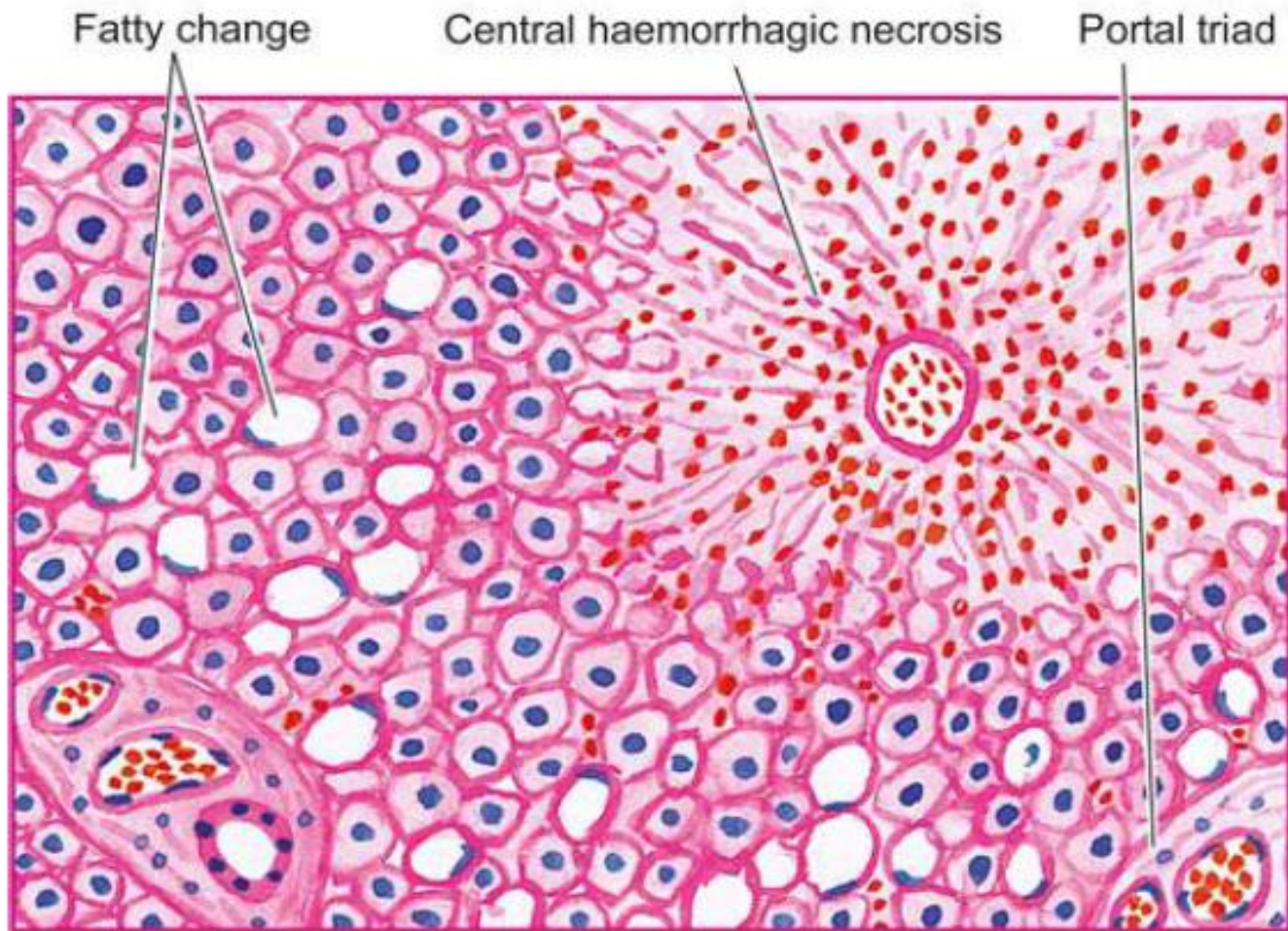
Thickened alveolar septa

Heart failure cells

Intra-alveolar RBCs



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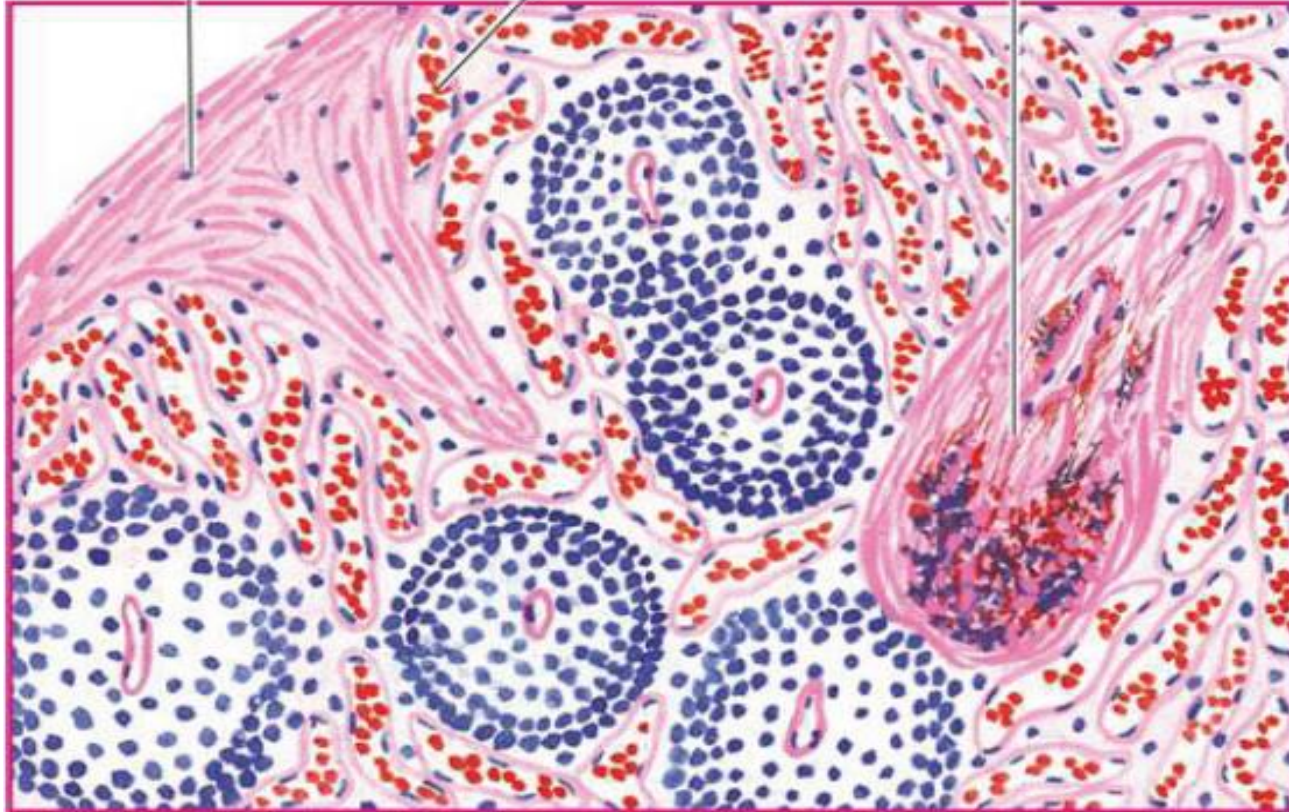




Thickened capsule

Congested sinusoids

Gamna-Gandy body



# POLLS 2

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Apoptosis & Necrosis*



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Inflammation*



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Haemodynamic Disorder*



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# Gandy gamma body is typically seen in chronic venous congestion of which of the following?

- (a) Lung
- (b) Kidney
- (c) Spleen
- (d) Liver

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**C**

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# Heart failure cells is typically seen in chronic venous congestion of which of the following?

- (a) Lung
- (b) Kidney
- (c) Spleen
- (d) Liver

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**A**

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# Nutmeg appearance is typically seen in chronic venous congestion of which of the following?

- (a) Lung
- (b) Kidney
- (c) Spleen
- (d) Liver

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**D**

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- **Oedema**
- **Hyperamia and congestion**
- **Thrombosis**
- **Embolism**
- **Ischemia**
- **Infaction**
- **Shock**

# **HEMOSTASIS**

- Hemostasis is a physiological process where by bleeding is stopped after injury, thus protecting the integrity of the vascular system after tissue injury.

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• Hemostasis involves →

➤ Platelets

➤ Clotting factors

➤ Endothelium at the site of vascular injury

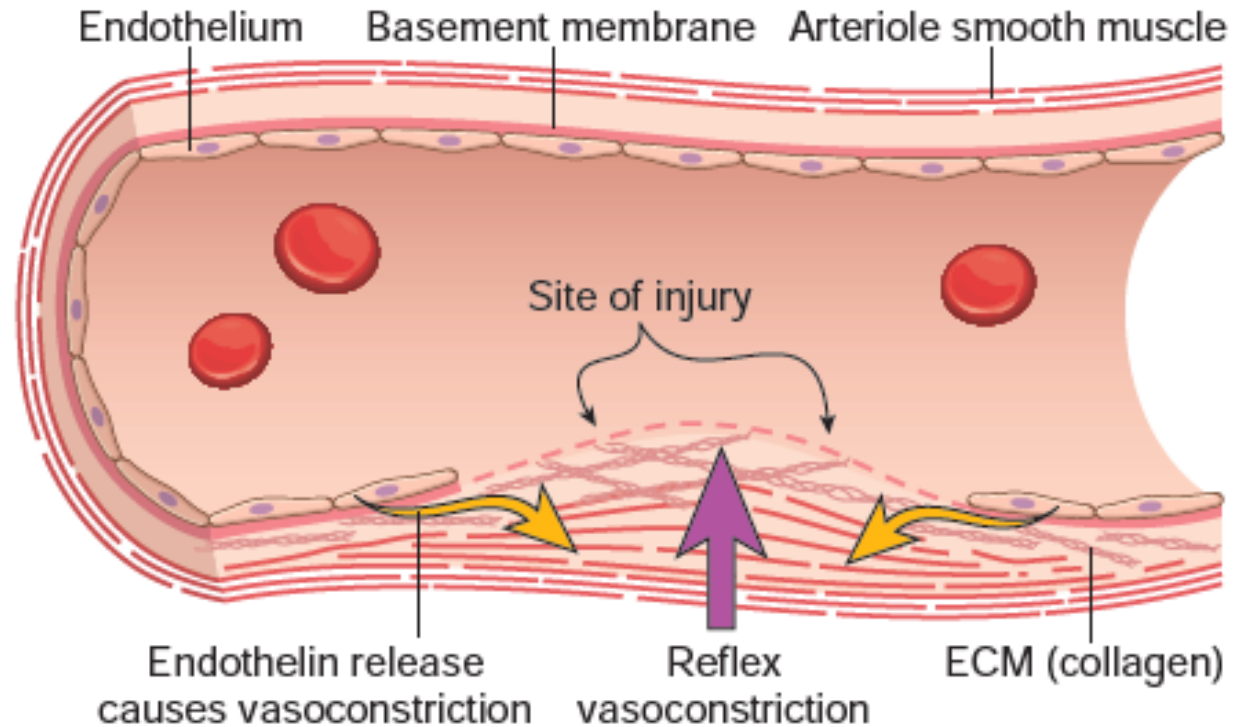


Results in the formation of a blood clot, which serves to prevent or limit the extent of bleeding.

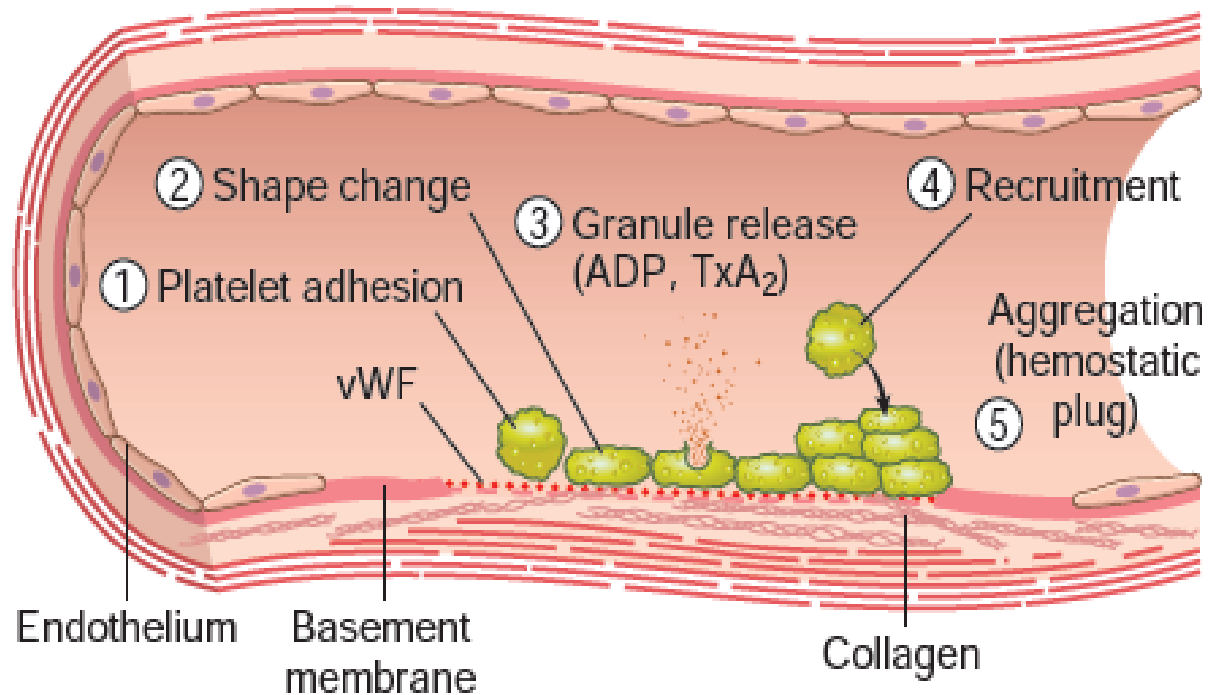
# **STEPS**

- 1.Arteriolar vasoconstriction**
- 2.Primary hemostasis**
- 3.Secondary hemostasis**
- 4.Clot stabilization and resorption**

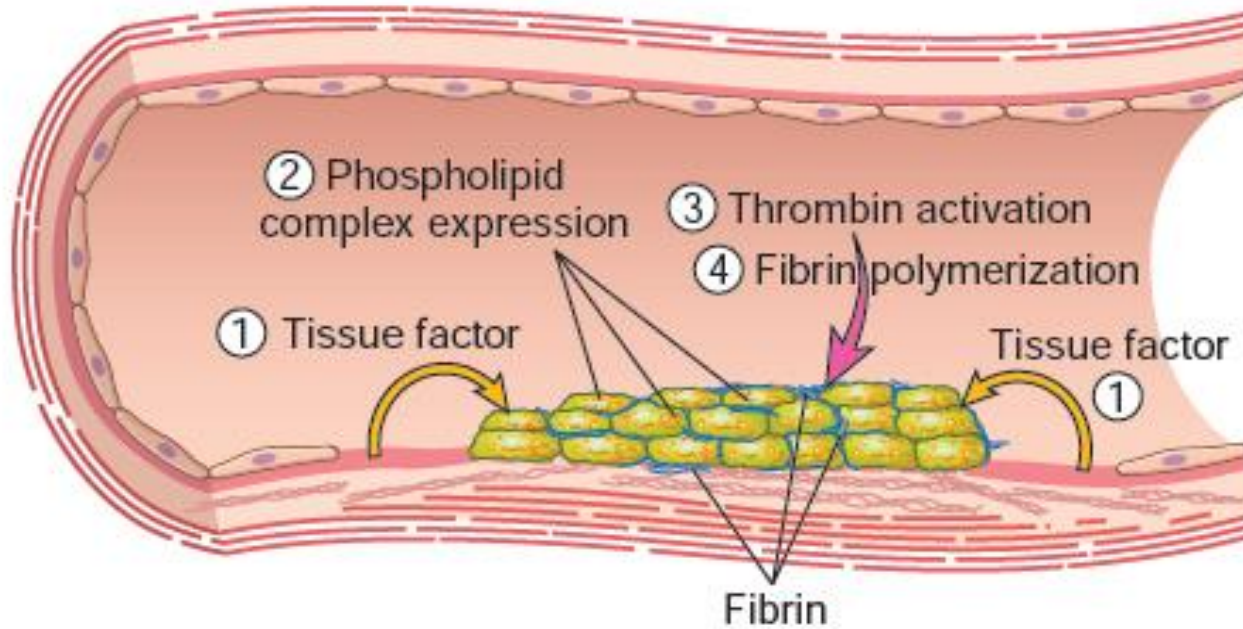
## A. VASOCONSTRICTION



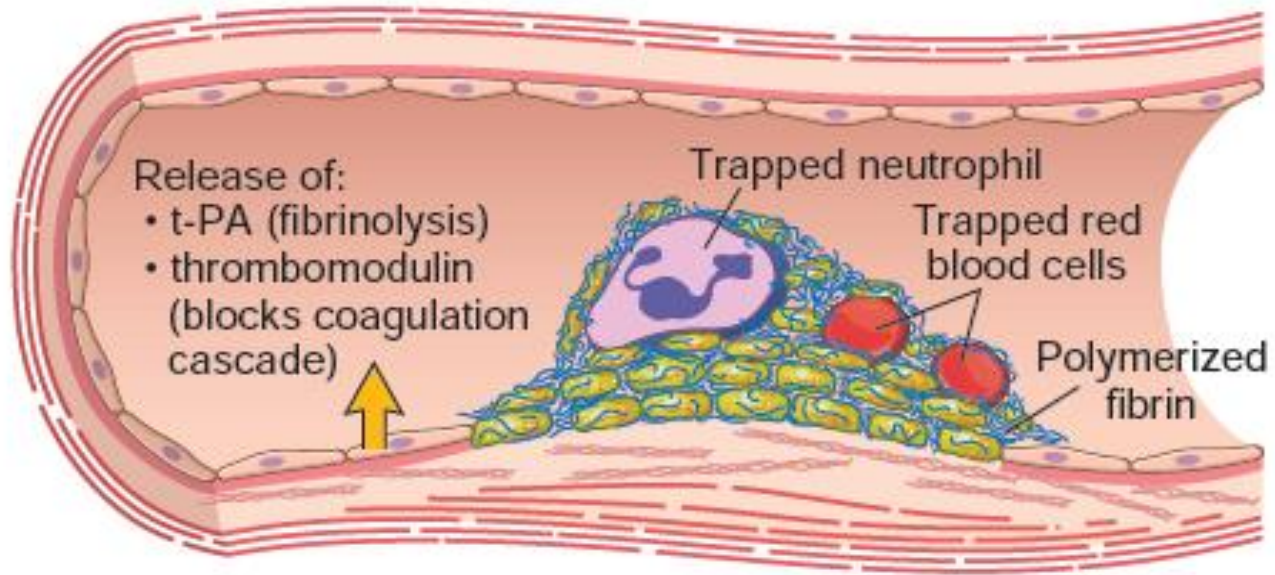
## B. PRIMARY HEMOSTASIS



## C. SECONDARY HEMOSTASIS



## D. THROMBUS AND ANTITHROMBOTIC EVENTS





# **STEPS**

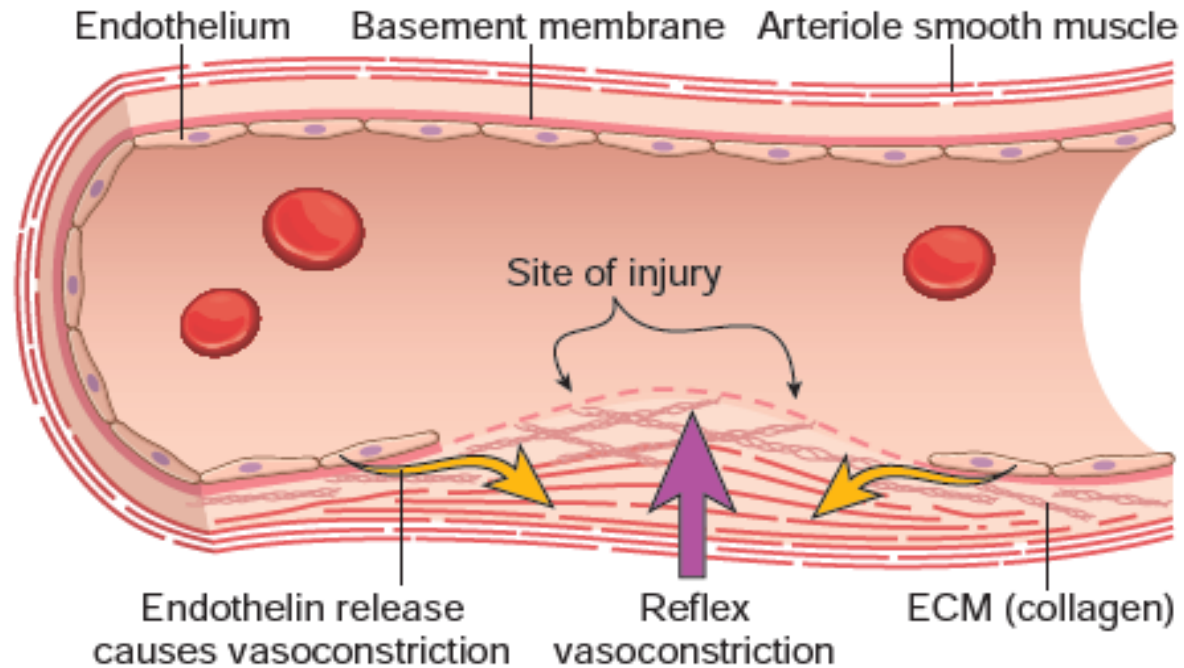
- 1.Arteriolar vasoconstriction**
- 2.Primary hemostasis**
- 3.Secondary hemostasis**
- 4.Clot stabilization and resorption**

# 1. Arteriolar vasoconstriction

- Occurs **immediately**
- Markedly reduces blood flow to the injured area
  1. It is mediated by **reflex neurogenic mechanisms**
  2. It is augmented by the local secretion of factors such as **endothelin**, a potent endothelium-derived vasoconstrictor.

- This effect is **transient**
- Bleeding would resume if not for activation of platelets and coagulation factors.

## A. VASOCONSTRICTION



# **STEPS**

- 1.Arteriolar vasoconstriction**
- 2.Primary hemostasis**
- 3.Secondary hemostasis**
- 4.Clot stabilization and resorption**

## **2. Primary hemostasis**

- **Primary hemostasis → the formation of the platelet plug**

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**Injury**



**Disruption of the endothelium**



**Exposes subendothelial von Willebrand factor (vWF) and collagen**



**1. Platelet adhesion**



**2. Platelet activation and release of secretory granules.**

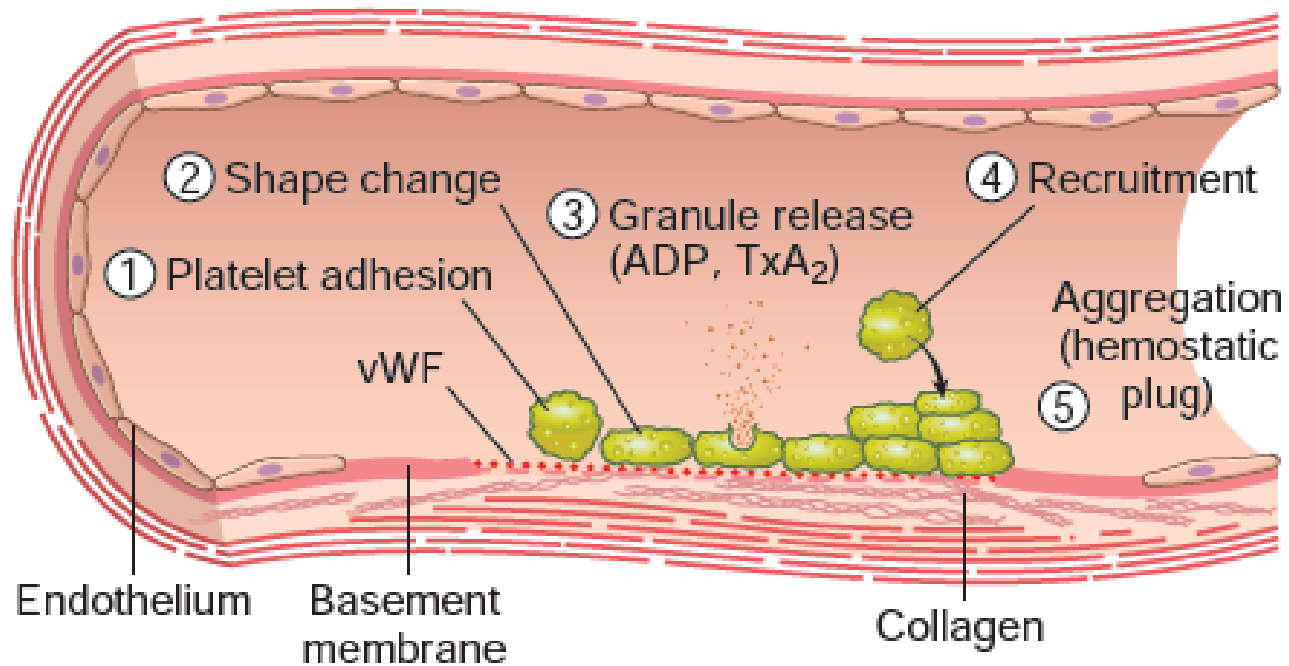


**3. Platelet aggregation/recruitment**

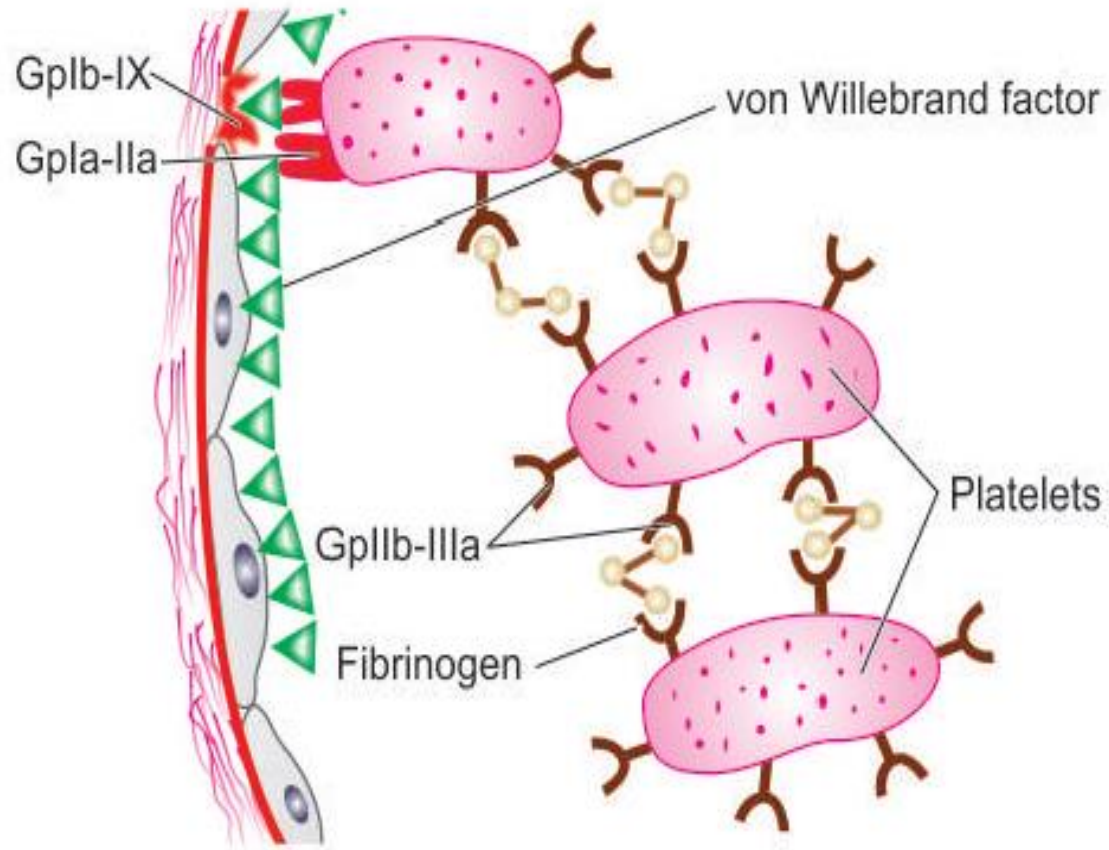


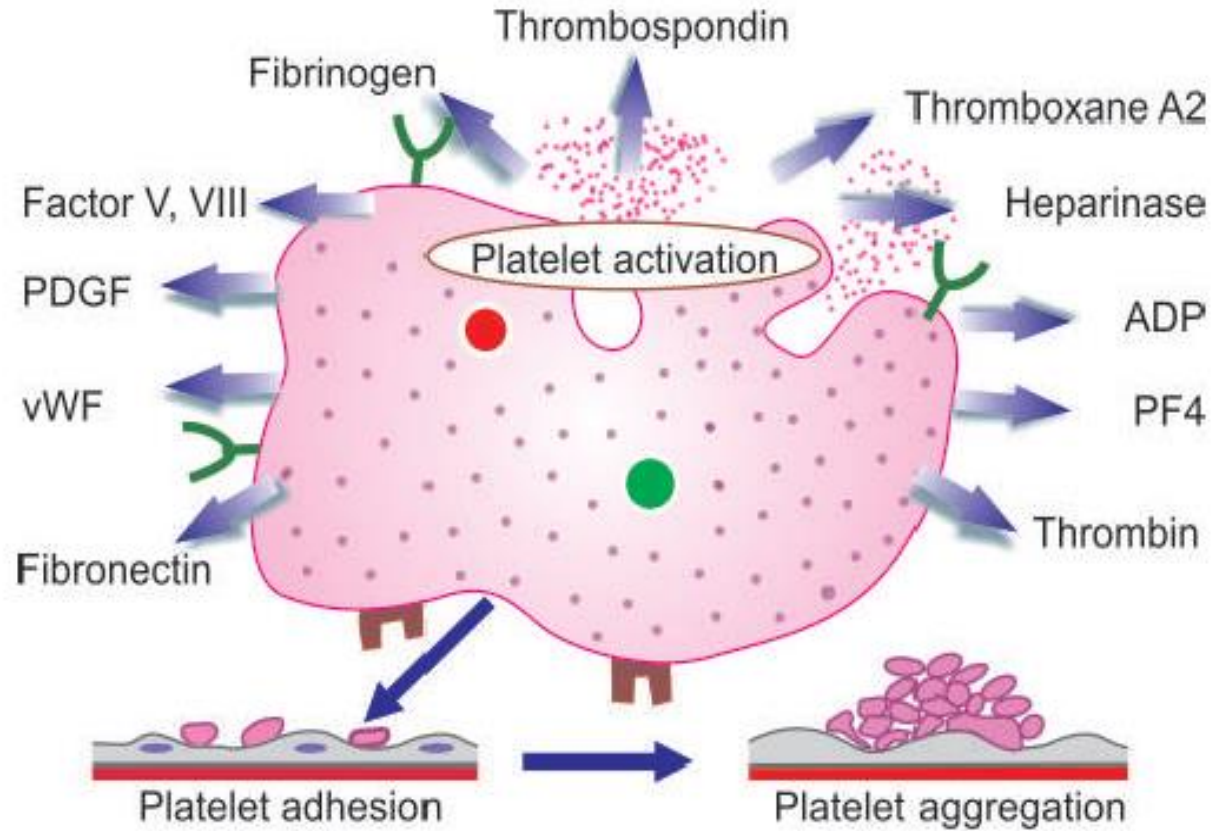
**Formation of primary hemostatic plug**

## B. PRIMARY HEMOSTASIS









# Platelet adhesion

- Platelets adhere to collagen in the subendothelium due to presence of receptor on platelet surface, glycoprotein **(Gp) Ia-IIa and Gp Ib-IX**
- The adhesion to the vessel wall is further stabilised by **von Willebrand factor**, an adhesion glycoprotein.
- Vwf forms a **bridge** between collagen of endothelium and platelet



# Platelet activation and Secretion

Three types of granules from their cytoplasm:

- **Dense granules**
- **$\alpha$ -granules**
- **Lysosomal vesicle**
- **i) Alpha granules:** Contain fibrinogen, fibronectin, factor V & VIII, PDGF, TGF-B and platelet factor 4.
- **ii) Dens bodies or delta-granules:** Contain *ADP, Ca* , *serotonin* and epinephrine.

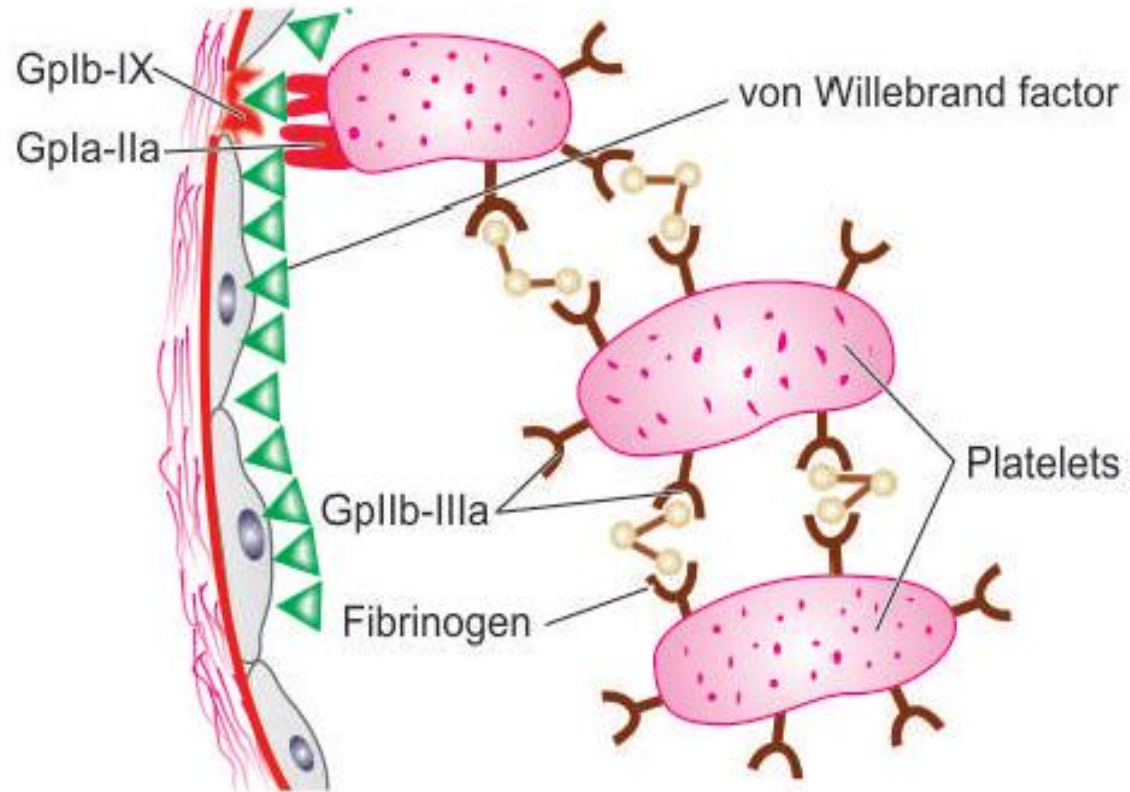
**Delta granules of platelets have**

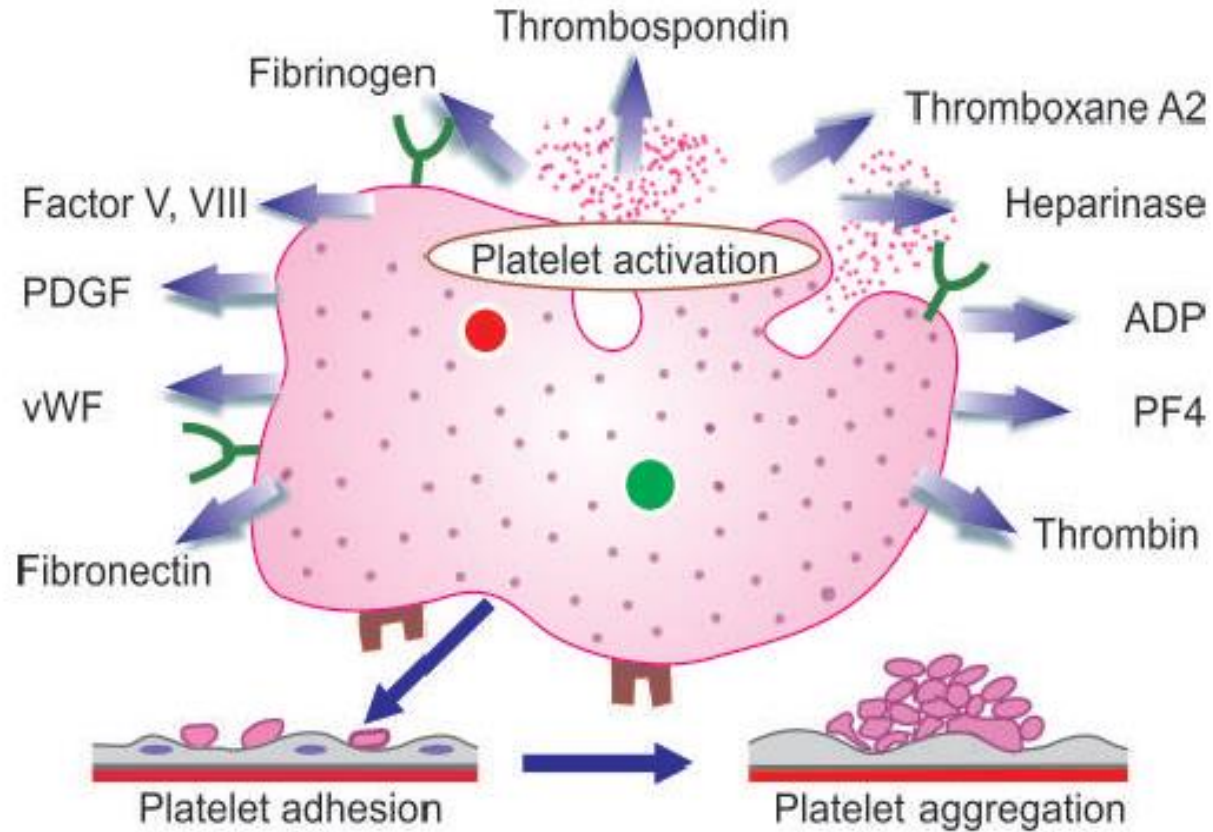
**A – ADP / ATP**

**C – Calcium**

**E – Epinephrine**

**S – Serotonin**

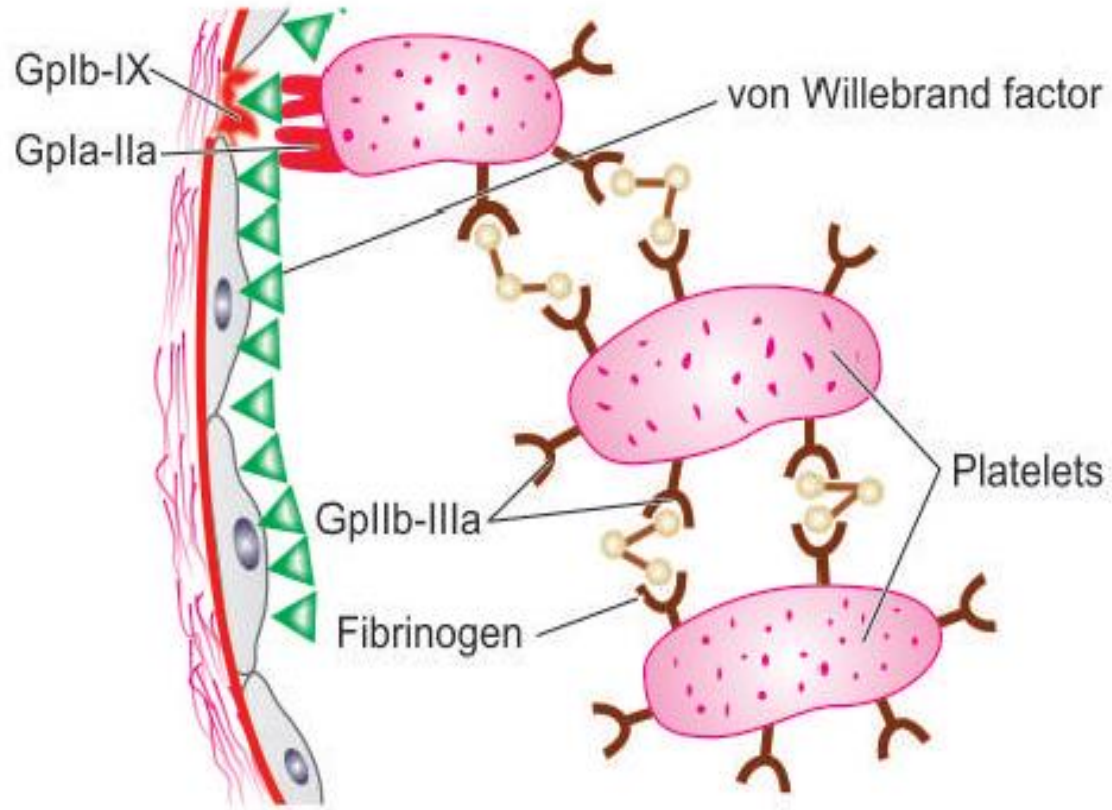






# Platelet aggregation

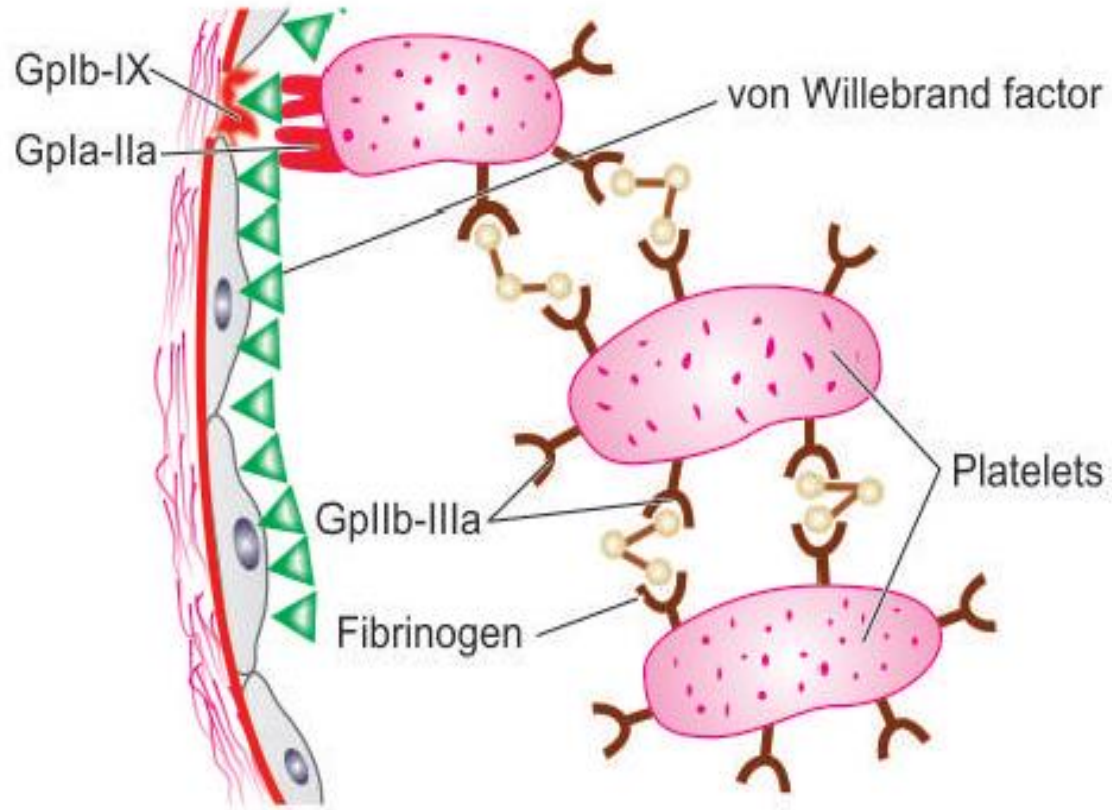
- Adherence of platelets to one another.
- This process is mediated by fibrinogen which forms **bridge between adjacent platelets** via glycoprotein receptors on platelets, **Gp IIb-IIIa**
- The most important endogenous stimulators of platelet aggregation are ADP and thromboxane A<sub>2</sub>
- It forms primary hemostatic plug which is reversible.
- After this coagulation system is activated forming a secondary (definitive) hemostatic plug which is irreversible



# DISORDERS OF PLATELET FUNCTIONS

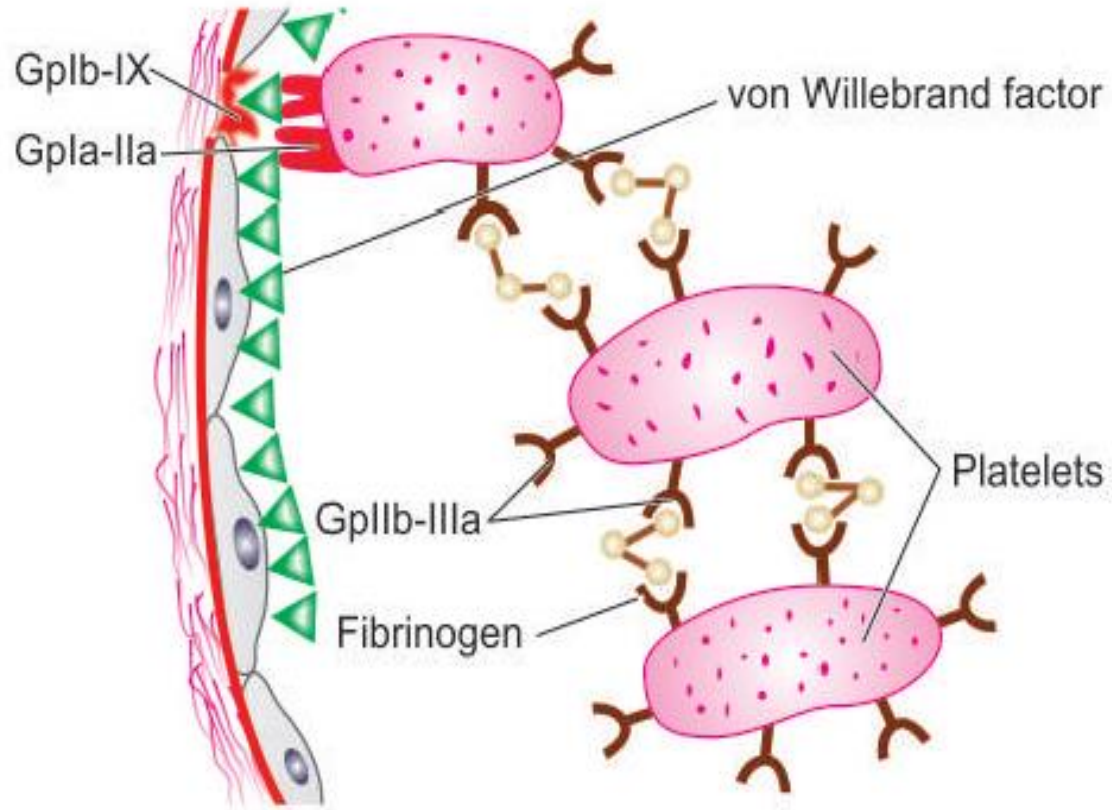
## DEFECTIVE PLATELET ADHESION

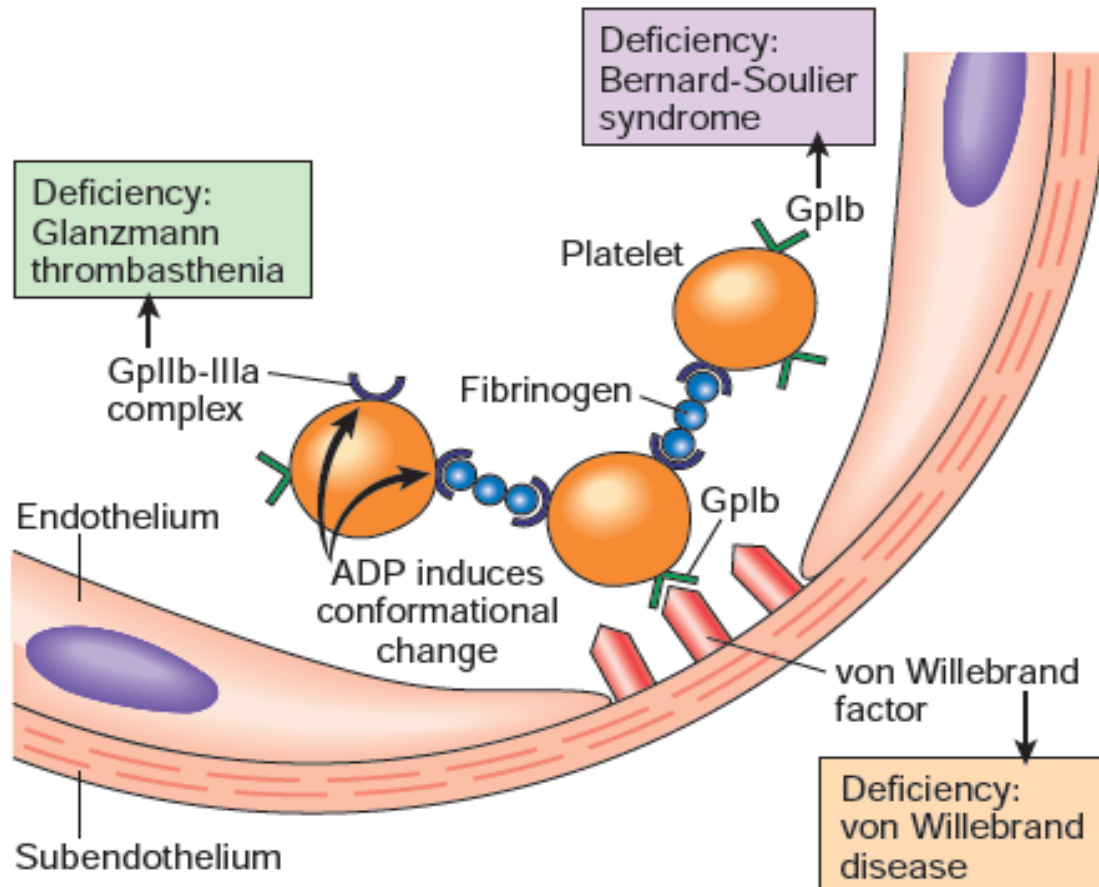
- **Bernard-Soulier syndrome** → an autosomal recessive disorder due to deficiency or dysfunction of **glycoprotein Ib-IIa**. Thus there is defect in platelet adhesion



## DEFECTIVE PLATELET AGGREGATION

- **Glanzmann's disease** → autosomal recessive disorder due to deficiency/dysfunction of **glycoprotein IIb-IIIa**. Thus there is defective platelet aggregation





# **STEPS**

- 1.Arteriolar vasoconstriction**
- 2.Primary hemostasis**
- 3.Secondary hemostasis**
- 4.Clot stabilization and resorption**



### 3. Secondary hemostasis

- Secondary hemostasis : **deposition of fibrin** (conversion of the soluble plasma fibrinogen into solid mass of insoluble fibrin)

**Injury**



**Tissue factor expressed by subendothelial cells in the vessel wall, is exposed or negatively charged surface**



**Tissue factor binds and activates factor VII or factor XII**



**A cascade of reactions set in motion (Intrinsic, extrinsic, common)**



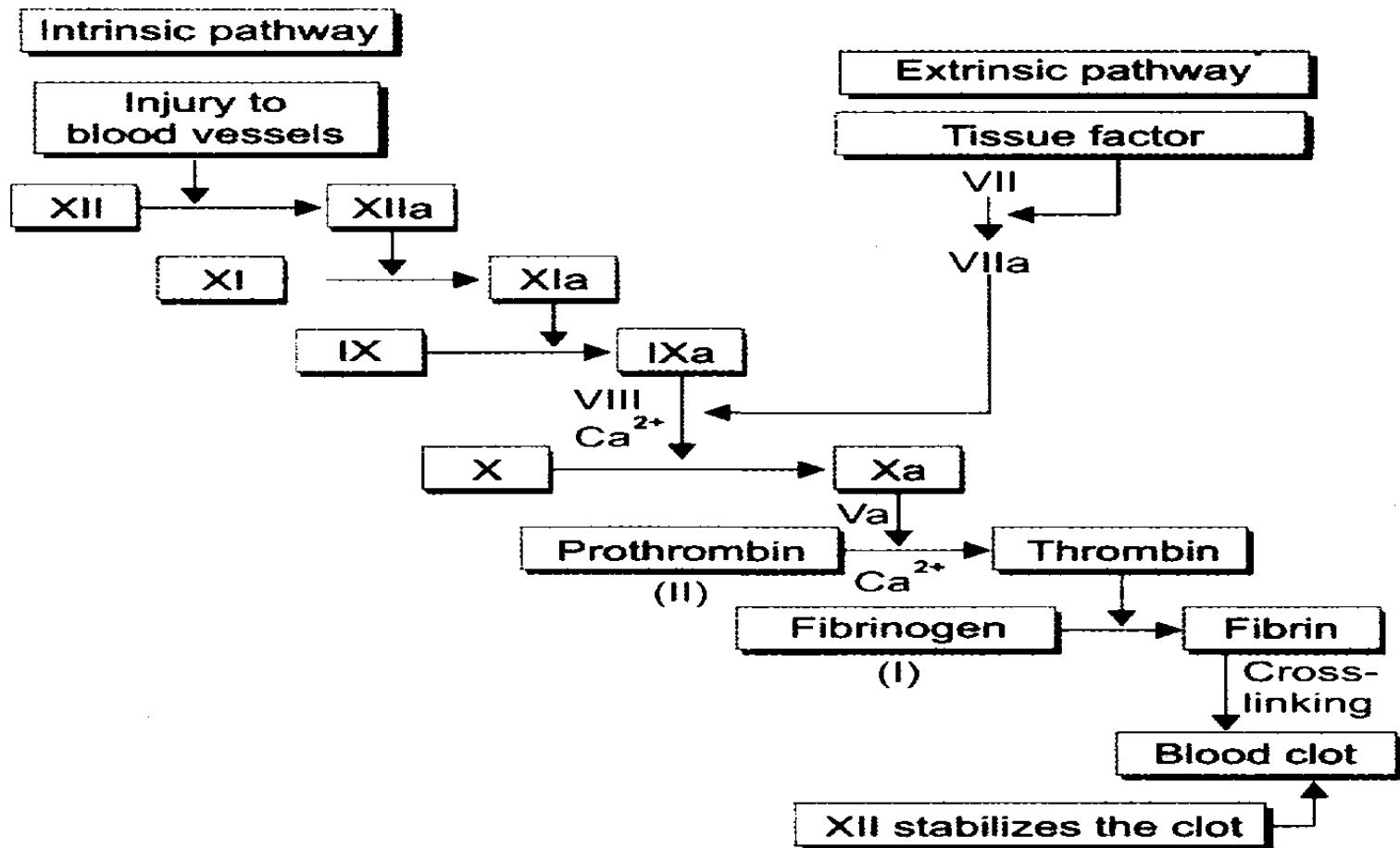
**fibrinogen into insoluble fibrin**

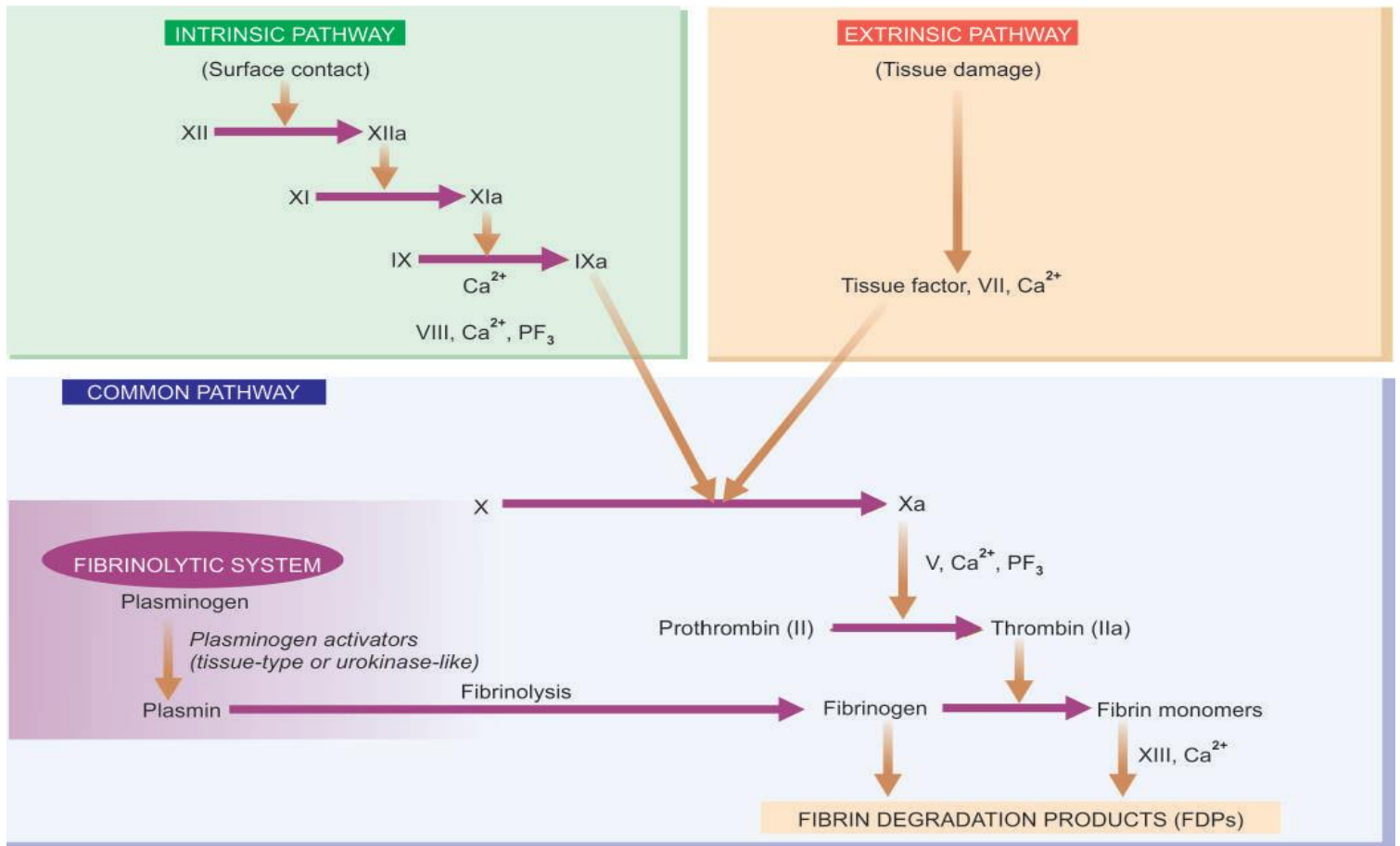


**fibrin meshwork is formed leading to additional platelet aggregation**

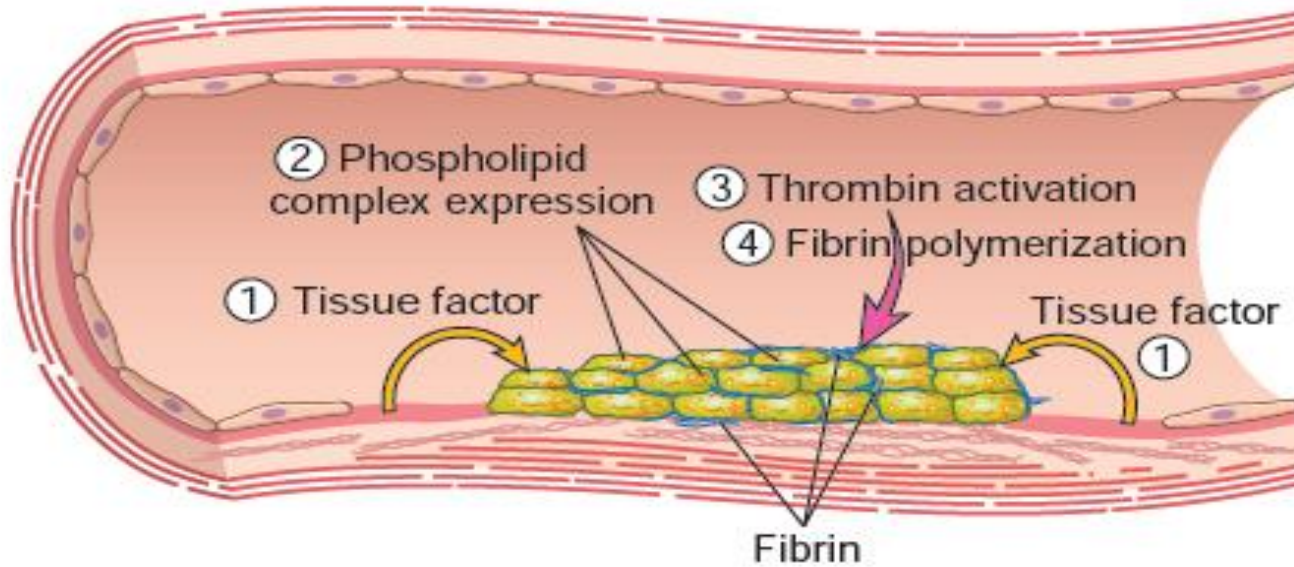


**Secondary hemostasis**



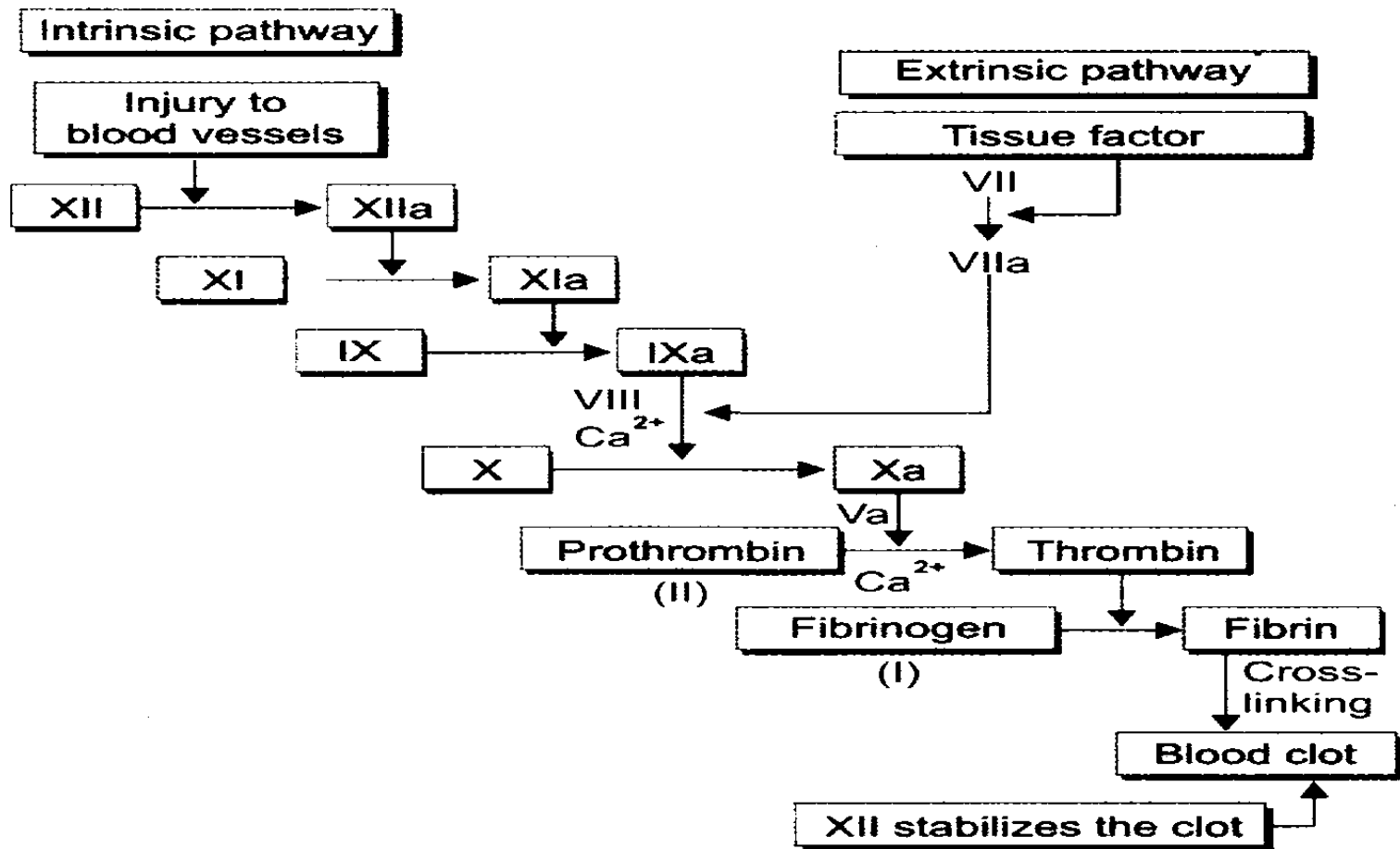


## C. SECONDARY HEMOSTASIS



# **In the intrinsic pathway**

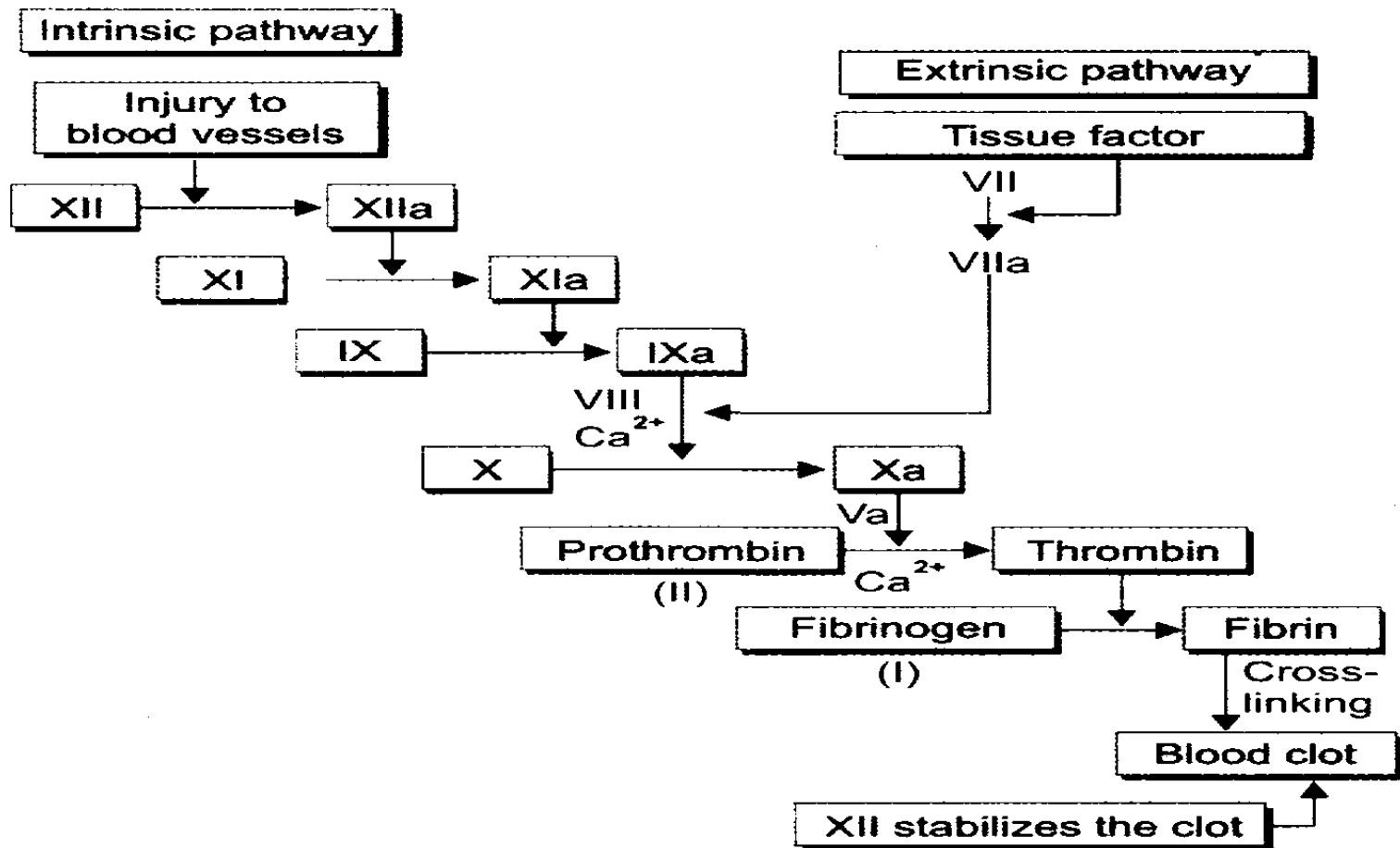
- contact with ECM in the subendothelium
- activation of factor XII
- the sequential interactions of factors XI, IX, VIII
- finally factor X, along with calcium ions (factor IV)



# **In the extrinsic pathway**

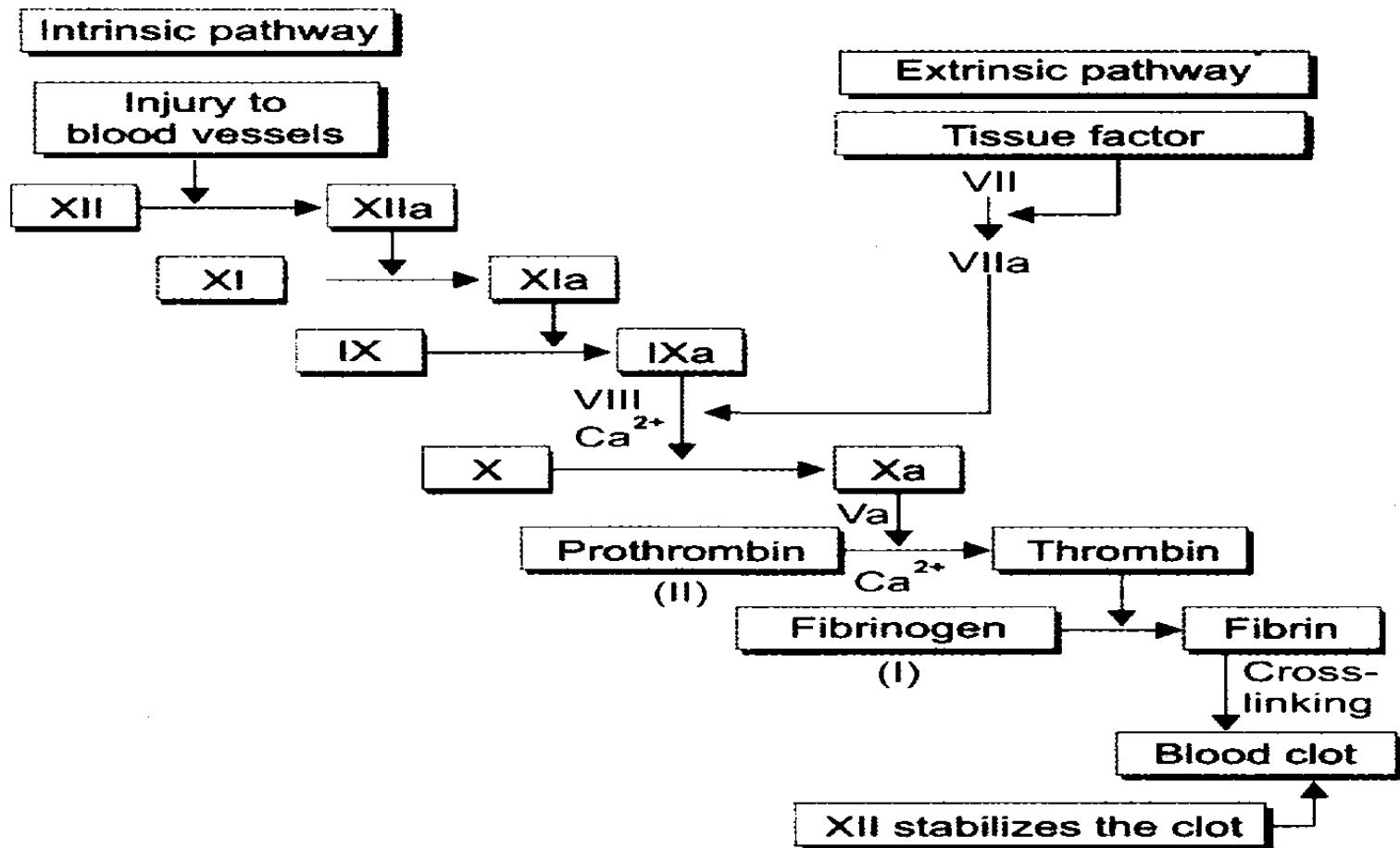
- Tissue damage results in release of tissue factor or thromboplastin
- Tissue factor on interaction with factor VII activates factor X.





# **The common pathway**

- Begins where both intrinsic and extrinsic pathways converge to activate factor X
- Factor X forms a complex with factor Va in the presence of calcium ions.
- This complex activates prothrombin (factor II) to thrombin (factor IIa)
- Thrombin converts fibrinogen to fibrin.



# **STEPS**

- 1.Arteriolar vasoconstriction**
- 2.Primary hemostasis**
- 3.Secondary hemostasis**
- 4.Clot stabilization and resorption**

## 4. Clot stabilization and resorption

Polymerized fibrin and platelet aggregates



Permanent plug that prevents further hemorrhage.



Counterregulatory mechanisms (tissue plasminogen activator, t-PA, thrombomodulin) are set into motion

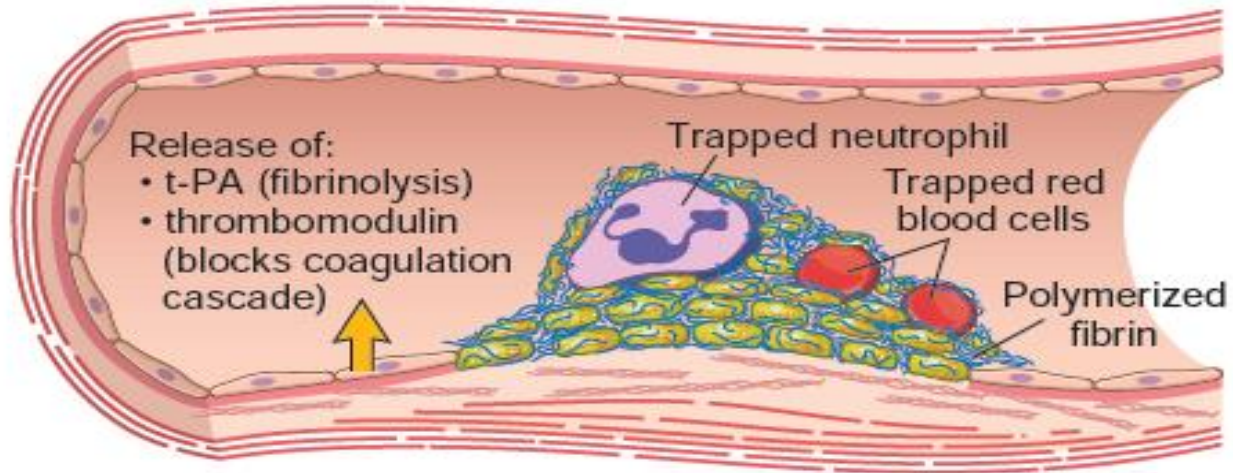


Blocks coagulation cascade



Clot resorption and tissue repair

## D. THROMBUS AND ANTITHROMBOTIC EVENTS

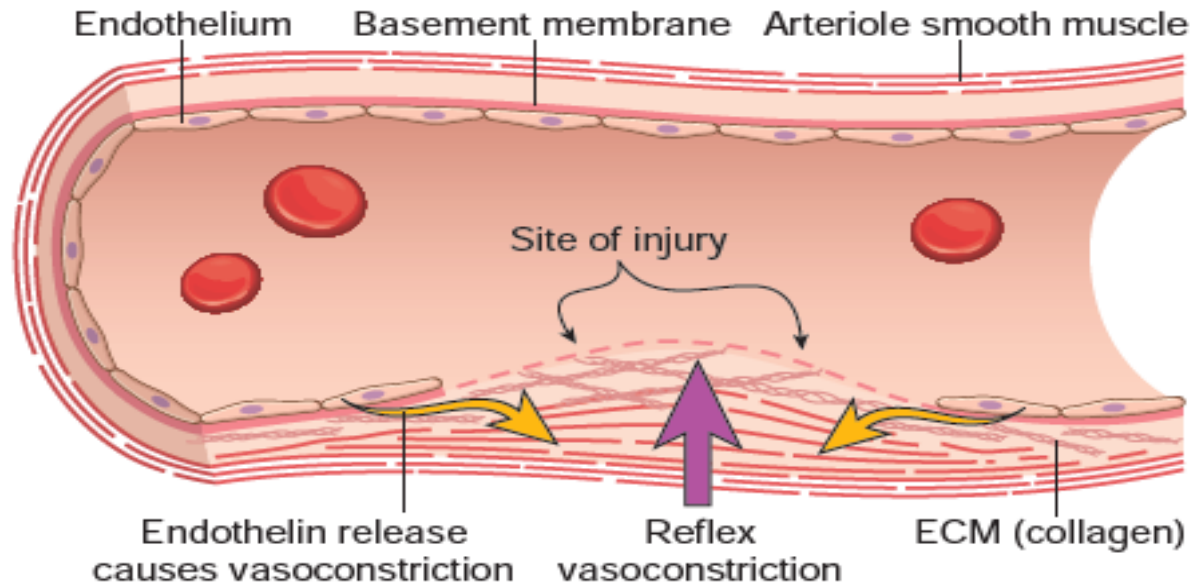


# REVISION



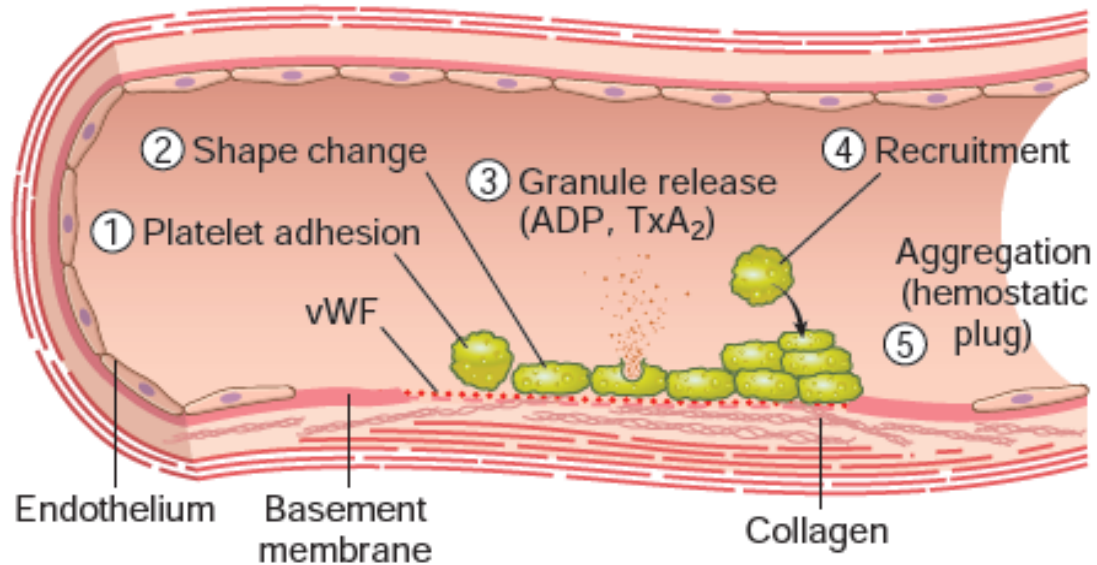
med[LIVE]

## A. VASOCONSTRICTION

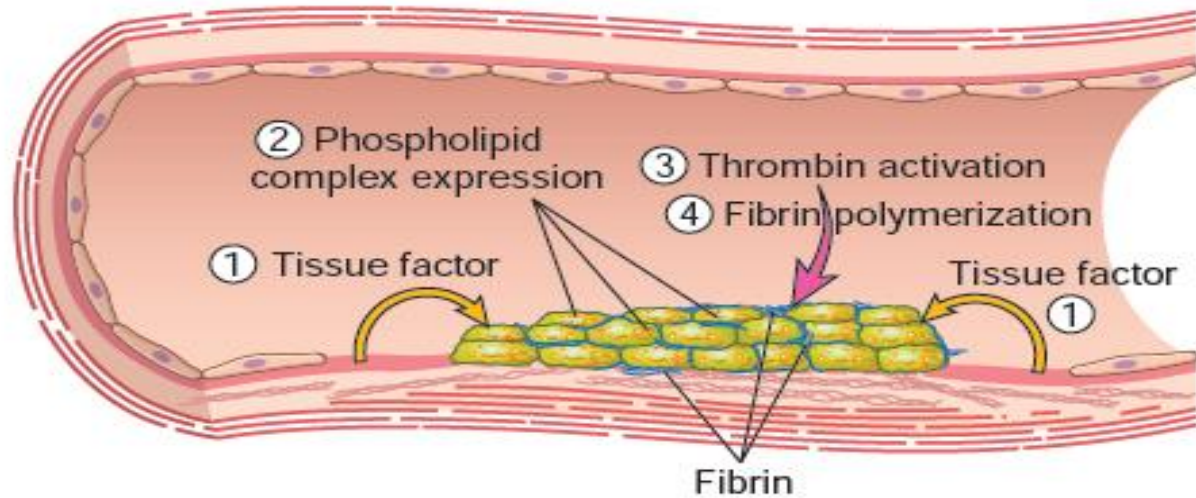




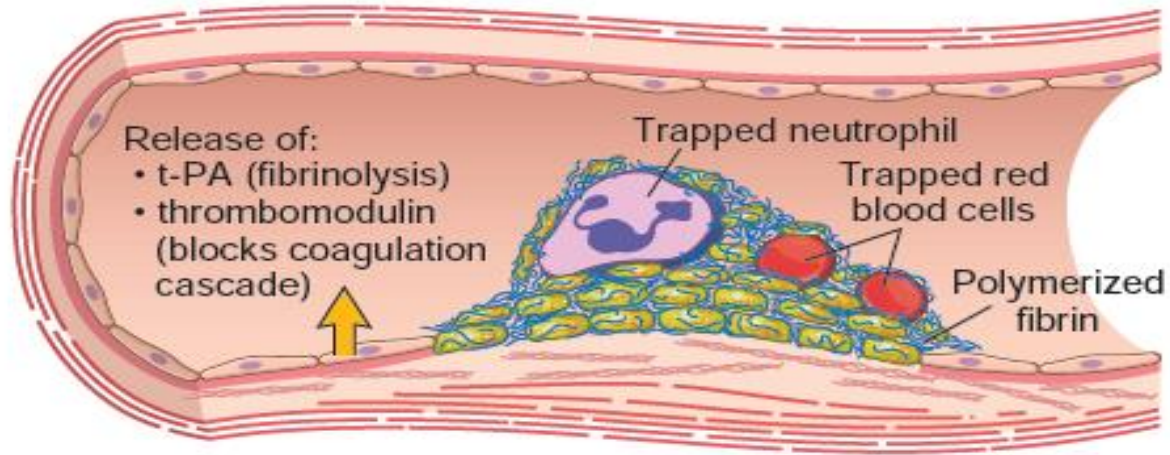
## B. PRIMARY HEMOSTASIS



### C. SECONDARY HEMOSTASIS



#### D. THROMBUS AND ANTITHROMBOTIC EVENTS



# POLLS 3

*Scan or Click to watch  
Cell Adaptation & Injury*



*Scan or Click to watch  
Apoptosis & Necrosis*



*Scan or Click to watch  
Inflammation*



*Scan or Click to watch  
Haemodynamic Disorder*



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**Following injury to a blood vessel, immediate haemostasis is achieved by-**

- a) Fibrin deposition
- b) Vasoconstriction
- c) Platelet adhesion
- d) Thrombosis

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**B**

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**The blood in the vessels normally does not clot because -**

- a) Vitamin K antagonists are present in plasma
- b) Thrombin has a positive feedback on plasminogen
- c) Sodium citrate in plasma chelates calcium ions
- d) Vascular endothelium is smooth and coated with glycocalyx

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**D**

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**Platelet Dense granules contain all except -**

- a) ADP
- b) 5-HT
- c) Calcium
- d) VwF

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**D**

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# **Platelet adhesion to collagen occurs via -**

- a) Factor VIII
- b) Factor IX
- c) Von-Willebrand factor
- d) Fibronectin

**C**

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**Which of the following is a procoagulation protein-**

- a) Thrombomodulin
- b) Protein C
- c) Protein S
- d) Thrombin

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**D**

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**Fibrin is degraded by -**

- a) Plasminogen
- b) Thromboplastin
- c) Plasmin
- d) FD

Dr. -

**C**

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All of the following are anticoagulant substances except

- (a) Antithrombin III
- (b) Protein S
- (c) vWF
- (d) Nitric oxide

Dr. PRIYANKA

**C**

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Which is not involved in local hemostasis?

- (a) Fibrinogen
- (b) Calcium
- (c) Vitamin K
- (d) Collagen

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**C**

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- **Oedema**
- **Hyperamia and congestion**
- **Thrombosis**
- **Embolism**
- **Ischemia**
- **Infaction**
- **Shock**

# THROMBOSIS

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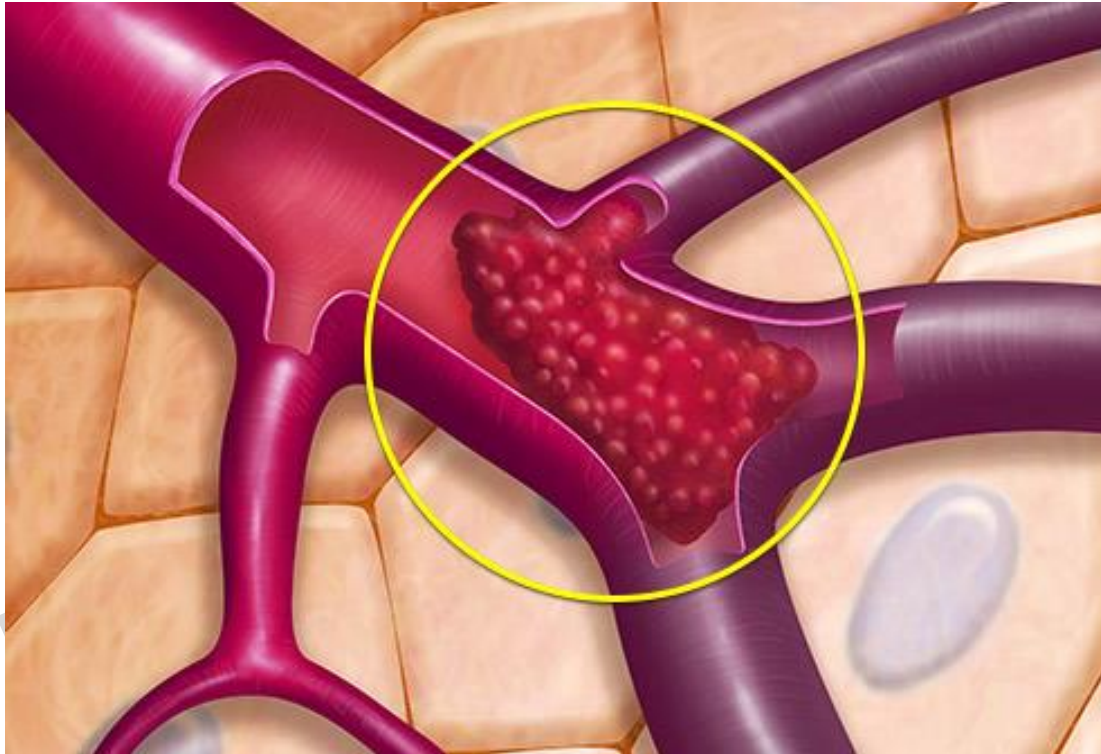
# OVERVIEW

- Definition
- Pathogenesis
- Types
- Gross
- Clinical features
- Differences between arterial and venous thrombosis
- Fate of thrombus

# Definition

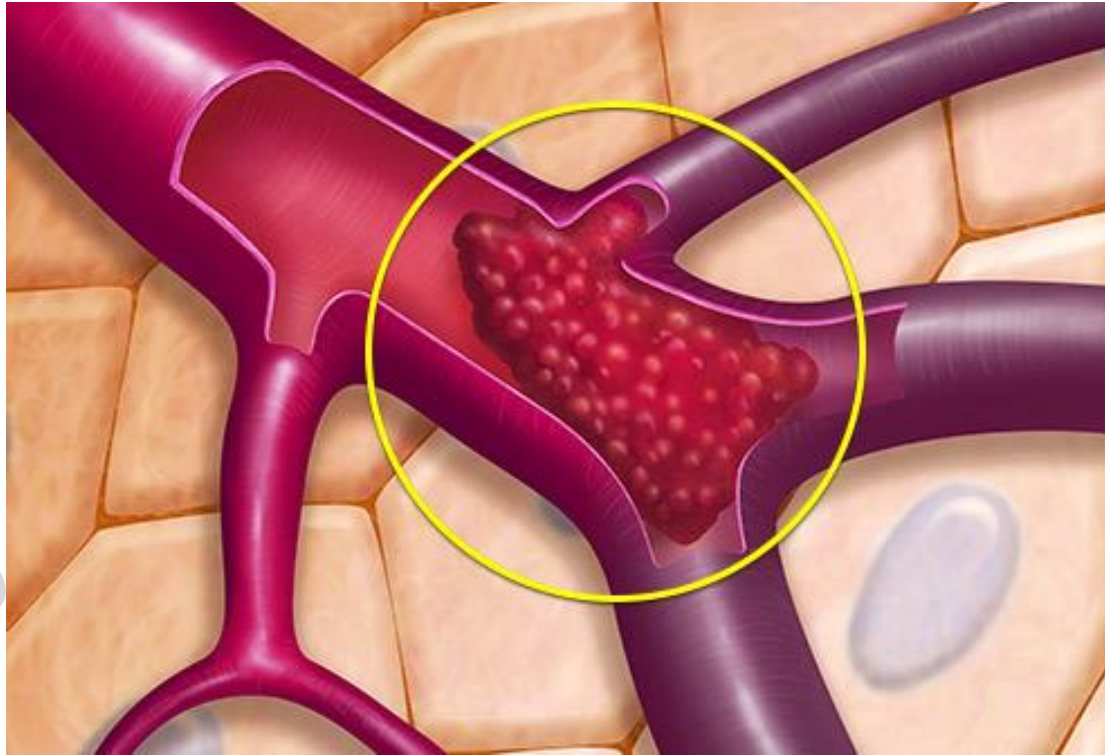
- Thrombosis is the formation of a blood clot (solid mass) inside a blood vessel or heart , from the constituents of flowing blood , obstructing the flow of blood through the circulatory system
- It is defined as the pathologic formation of intravascular fibrin-platelet thrombus
- The mass itself is called a **thrombus**



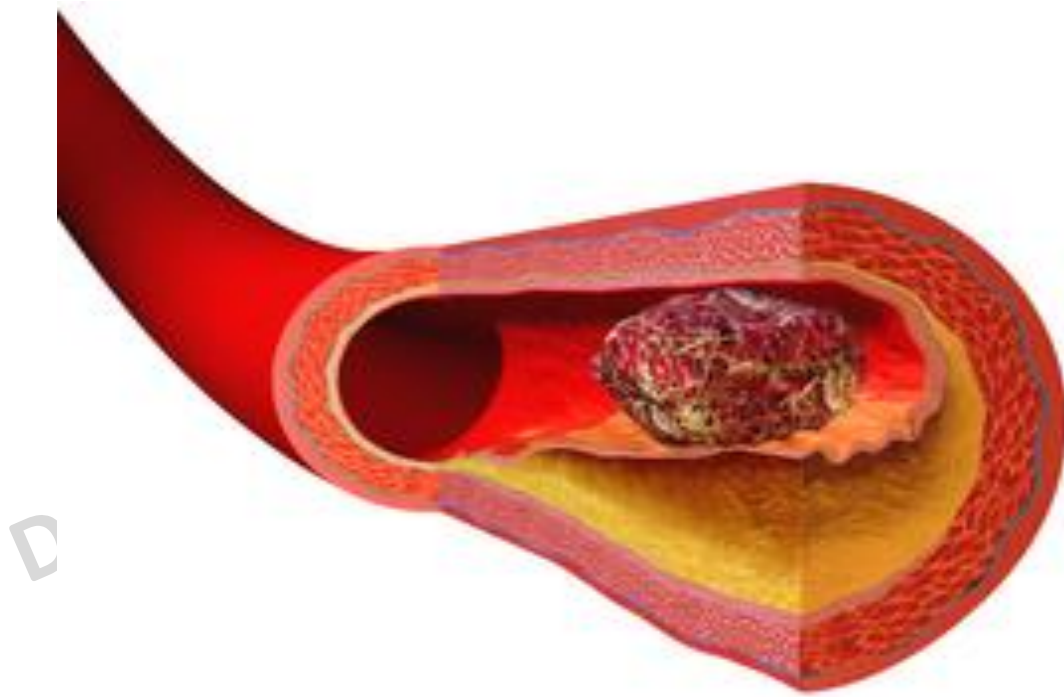


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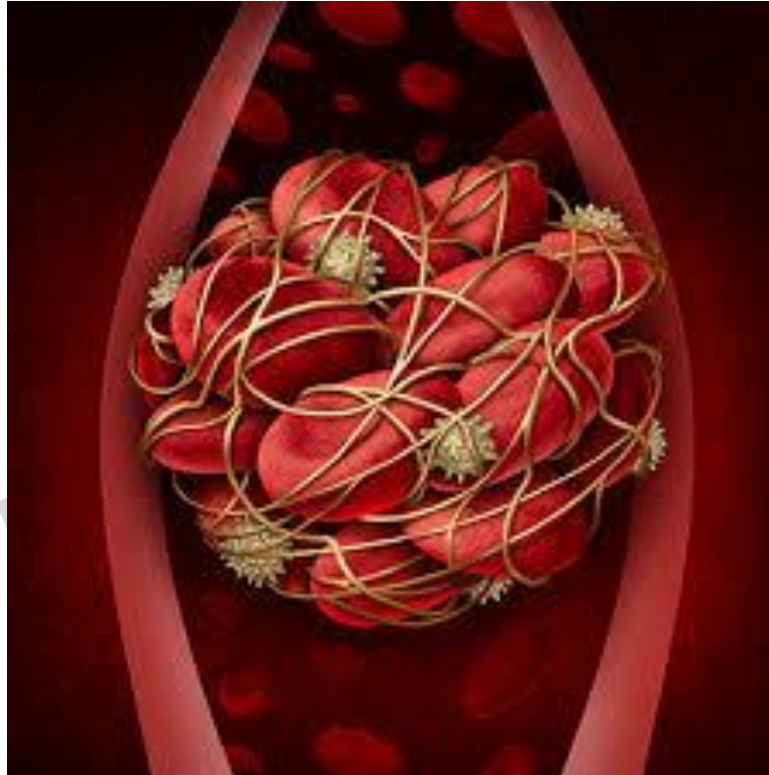
- **Haemostasis** occurs after injury to CVS and is useful as it stop escape of blood and plasma,
- **Thrombosis** occurs in the unruptured CVS (without injury) and has harmful effects of ischemia



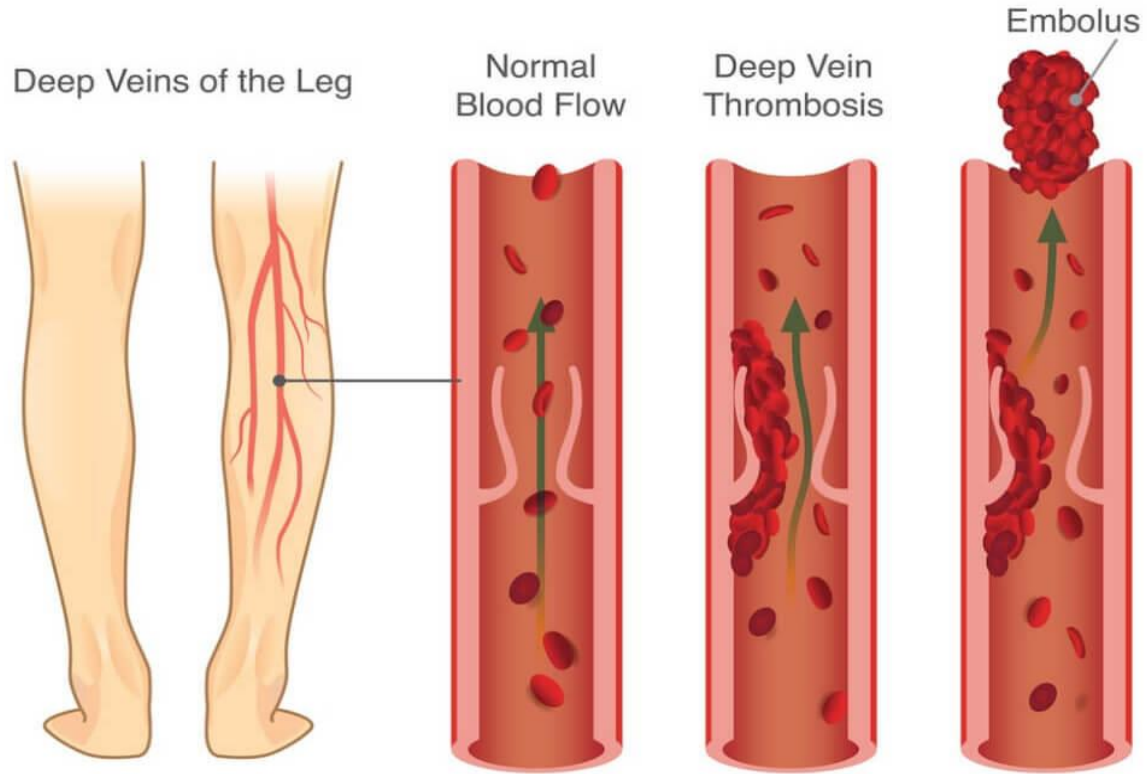
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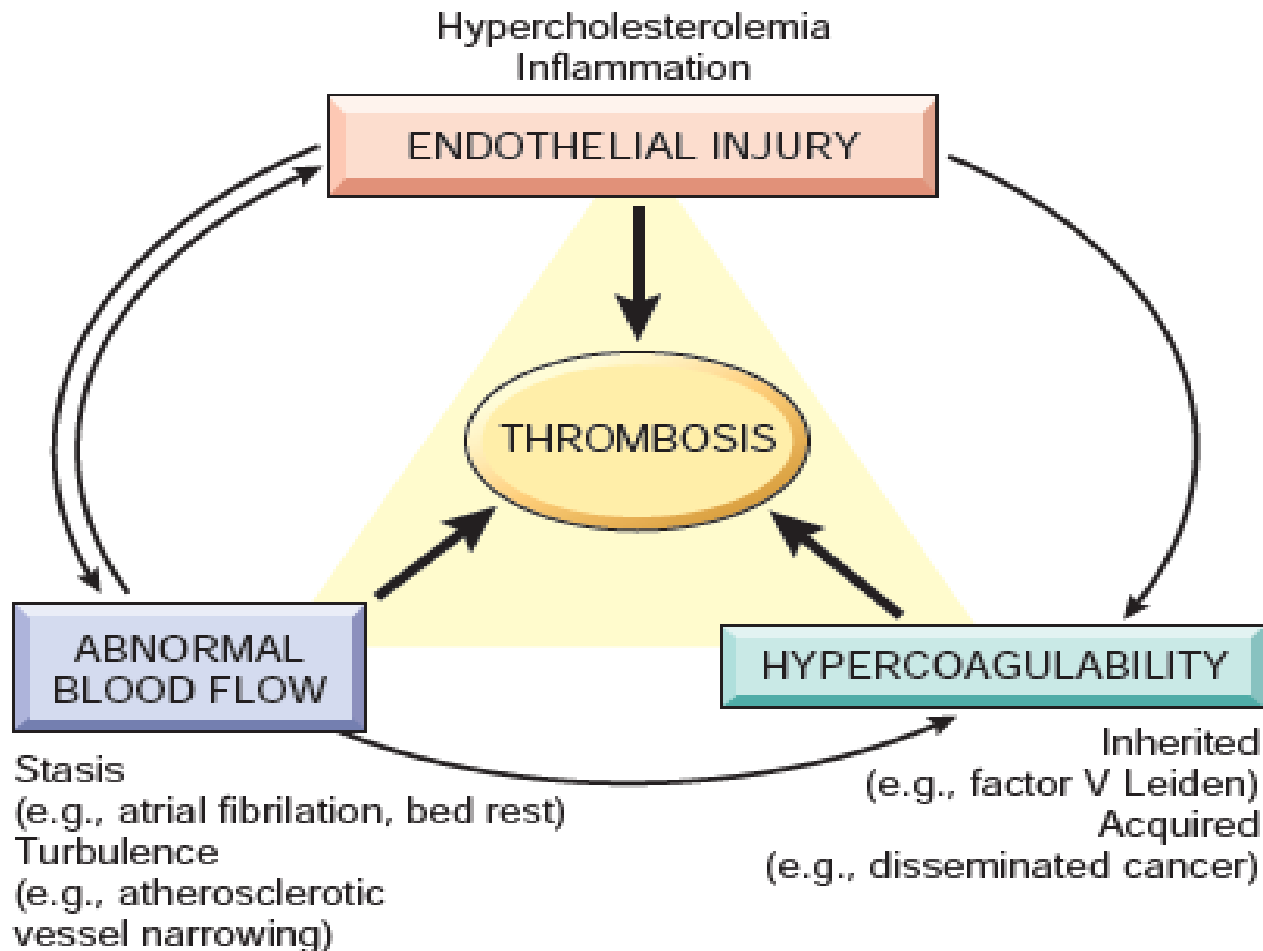
# OVERVIEW

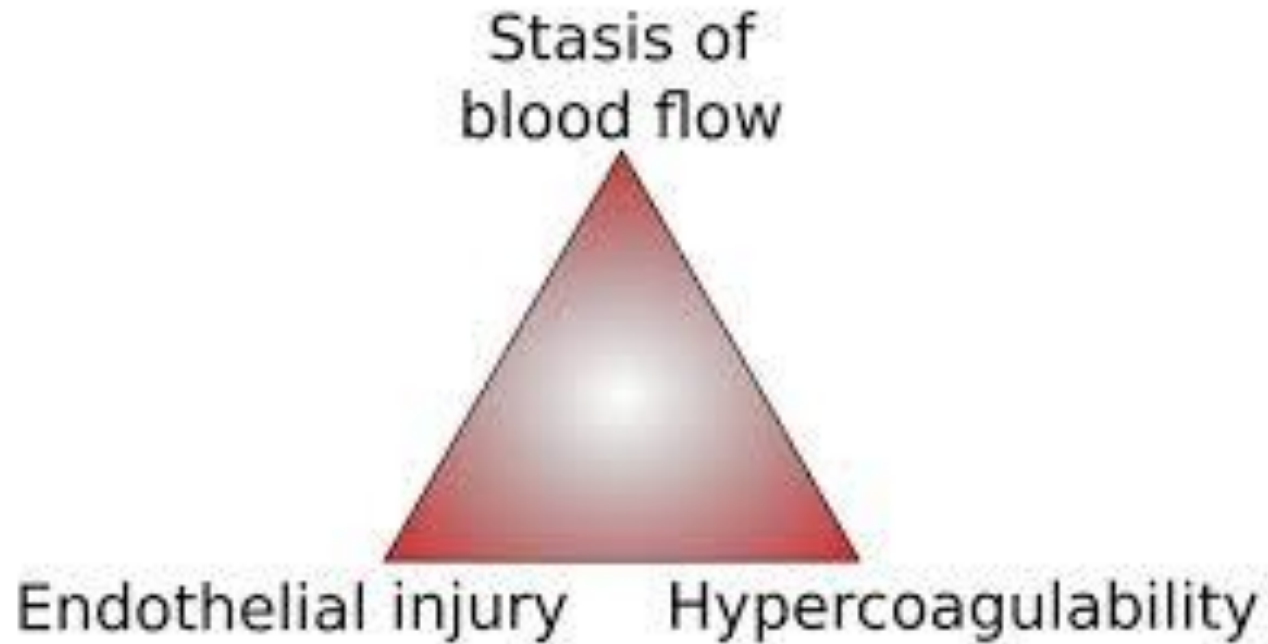
- Definition
- Pathogenesis
- Types
- Gross
- Clinical features
- Differences between arterial and venous thrombosis
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# Pathophysiology

- Virchow described three primary events which predispose to thrombus formation (**Virchow's triad**):
  - ✓ Endothelial injury →
    - Activation of platelets
    - Activation of clotting system
  - ✓ Altered blood flow
  - ✓ Hypercoagulability of blood.

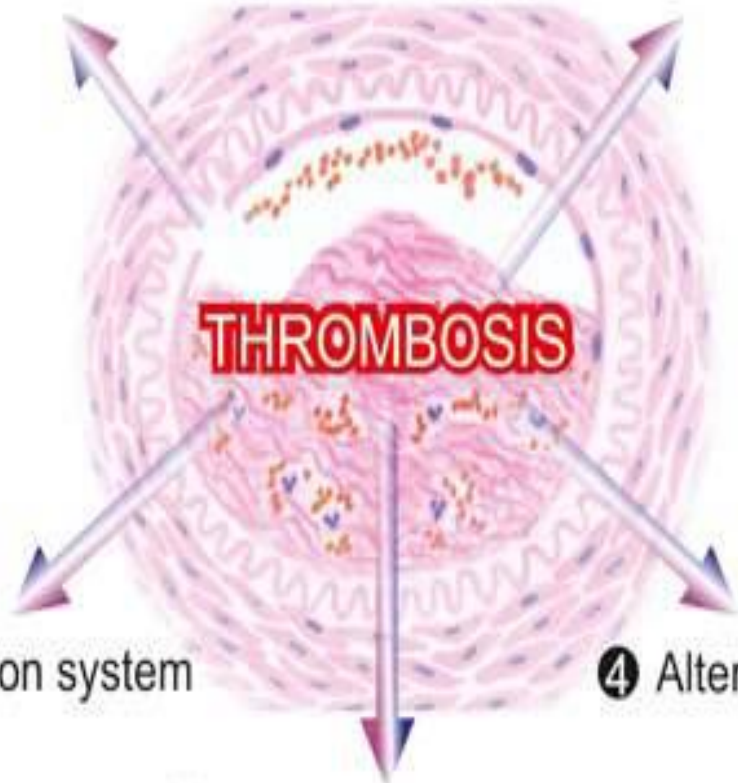






① Endothelial injury

② Role of platelets



③ Coagulation system

④ Altered blood flow

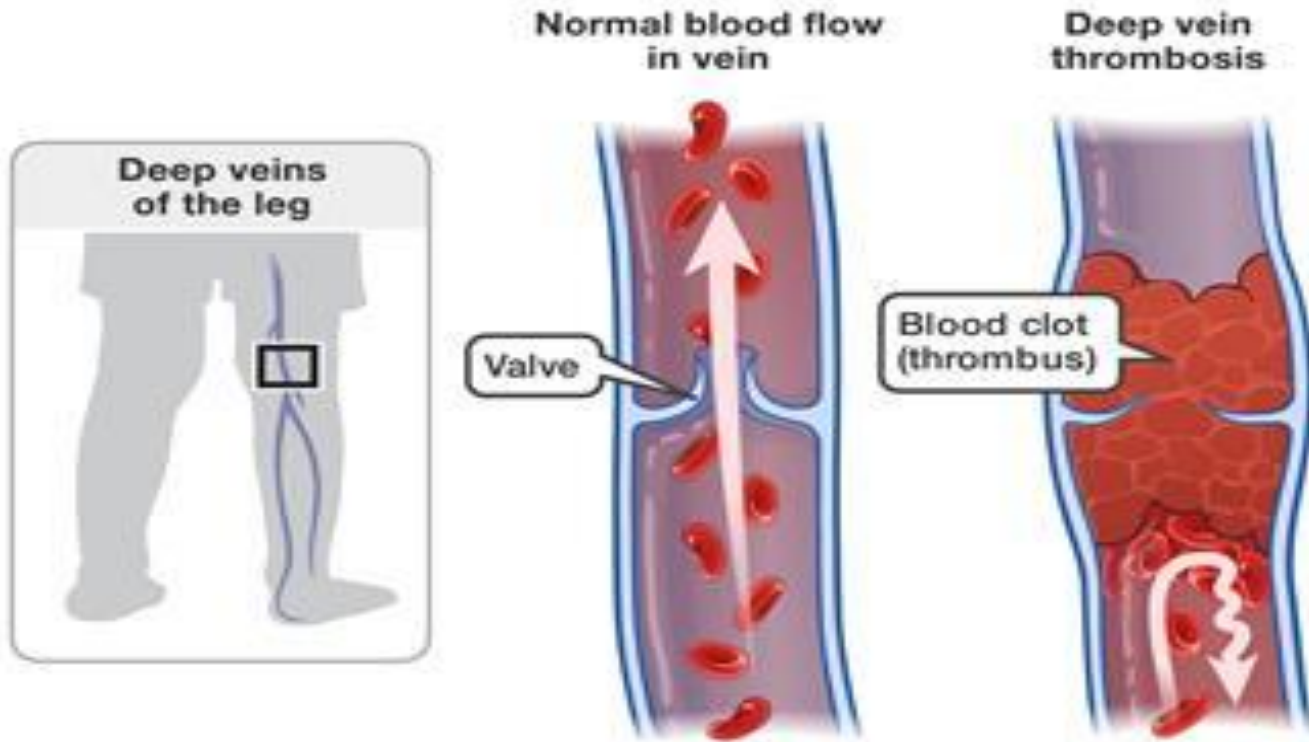
⑤ Hypercoagulability

**Virchow's triad = Endothelial injury + Alterations in the normal blood flow + Blood hypercoagulability**

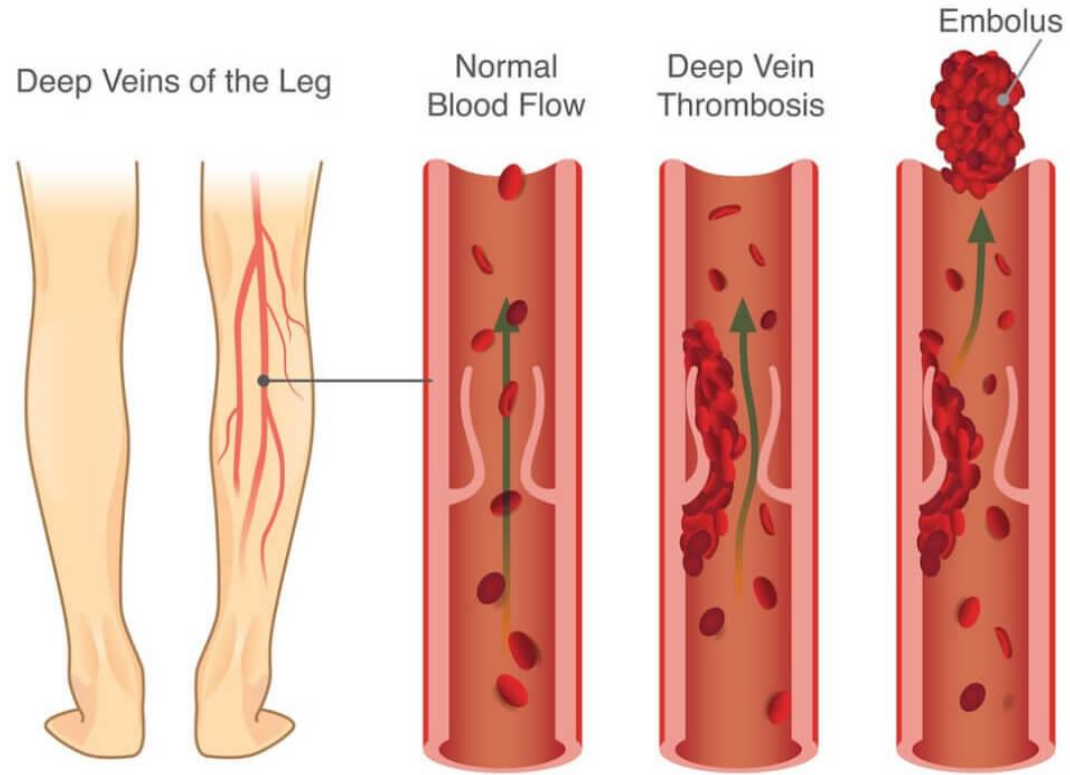
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# ENDOTHELIAL INJURY

- The integrity of blood vessel wall is important for maintaining normal blood flow
- Intact endothelium has both **antithrombotic property and prothrombotic property** → So no thrombosis



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# Prothrombotic

- **Thromboplastin or tissue factor** released from endothelial cells.
- **Von Willebrand factor** that causes adherence of platelets to the subendothelium.
- **Platelet activating factor** which is activator and aggregator of platelets.
- **Inhibitor of plasminogen activator** that suppresses fibrinolysis.



# Antithrombotic

- **Heparin-like substance** which accelerates the action of antithrombin III and inactivates some other clotting factors.
- **Thrombomodulin** which converts thrombin into activator of protein C, an anticoagulant.
- **Tissue plasminogen activator** which accelerates fibrinolytic activity.
- **Inhibitors of platelet aggregation** such as ADPase, PGI<sub>2</sub> (or prostacyclin).

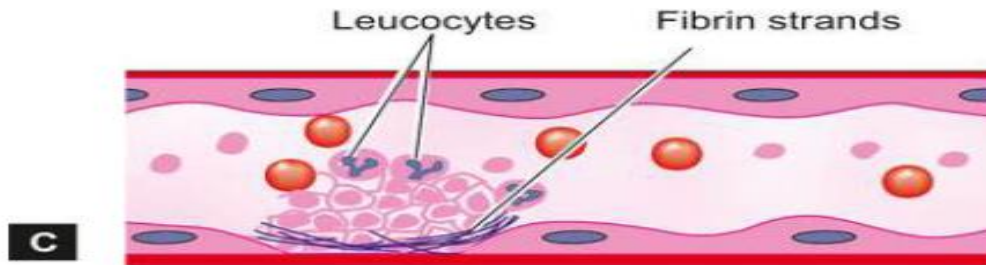
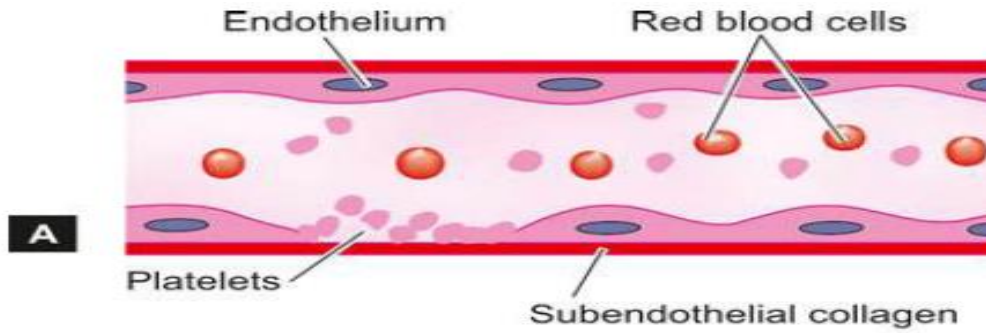
**Endothelial injury**



**Exposes vWF and tissue factor  
(prothrombotic)**



**Thrombosis**



# Pathophysiology

- Virchow described three primary events which predispose to thrombus formation (**Virchow's triad**):

- ✓ Endothelial injury →

Activation of platelets

Activation of clotting system

- ✓ Altered blood flow

- ✓ Hypercoagulability of blood.

# **ACTIVATION OF PLATELETS**

- After endothelial injury platelets come in contact with subendothelial ECM especially collagen
- causes three reactions in platelets →

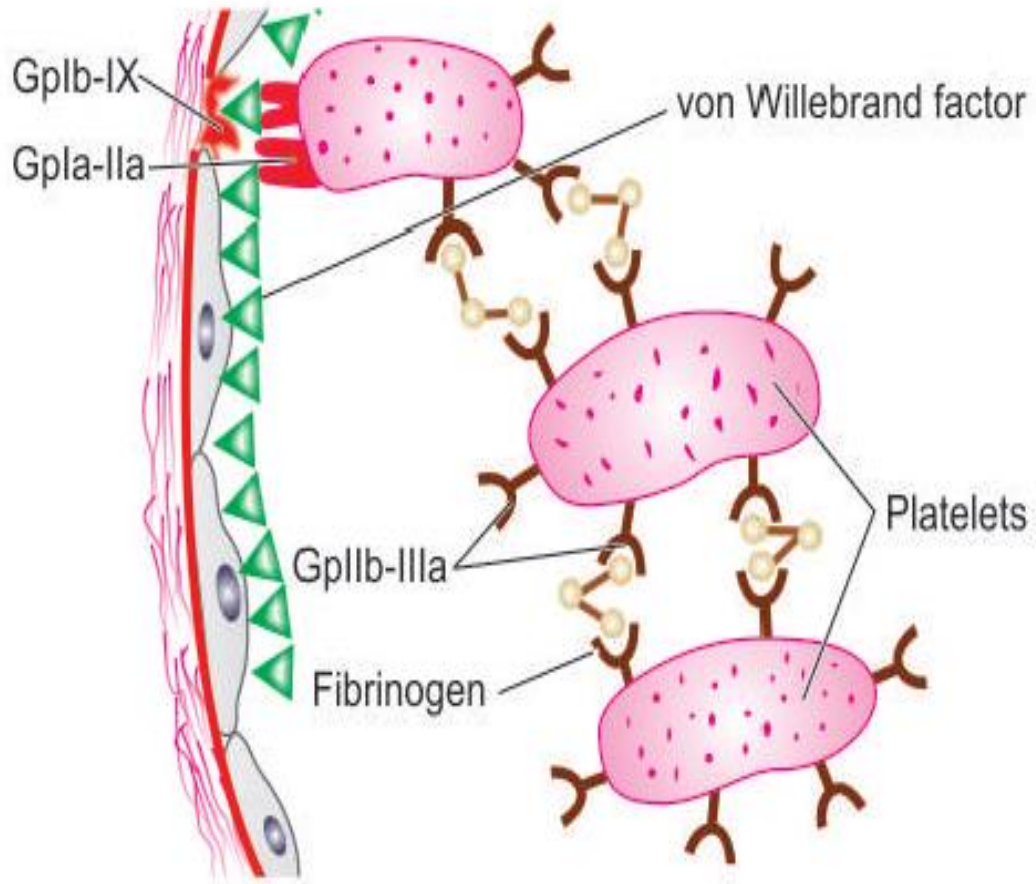
**1. Platelet adhesion**

**2. Platelet activation and Secretion**

**3. Platelet aggregation**

# 1. Platelet adhesion

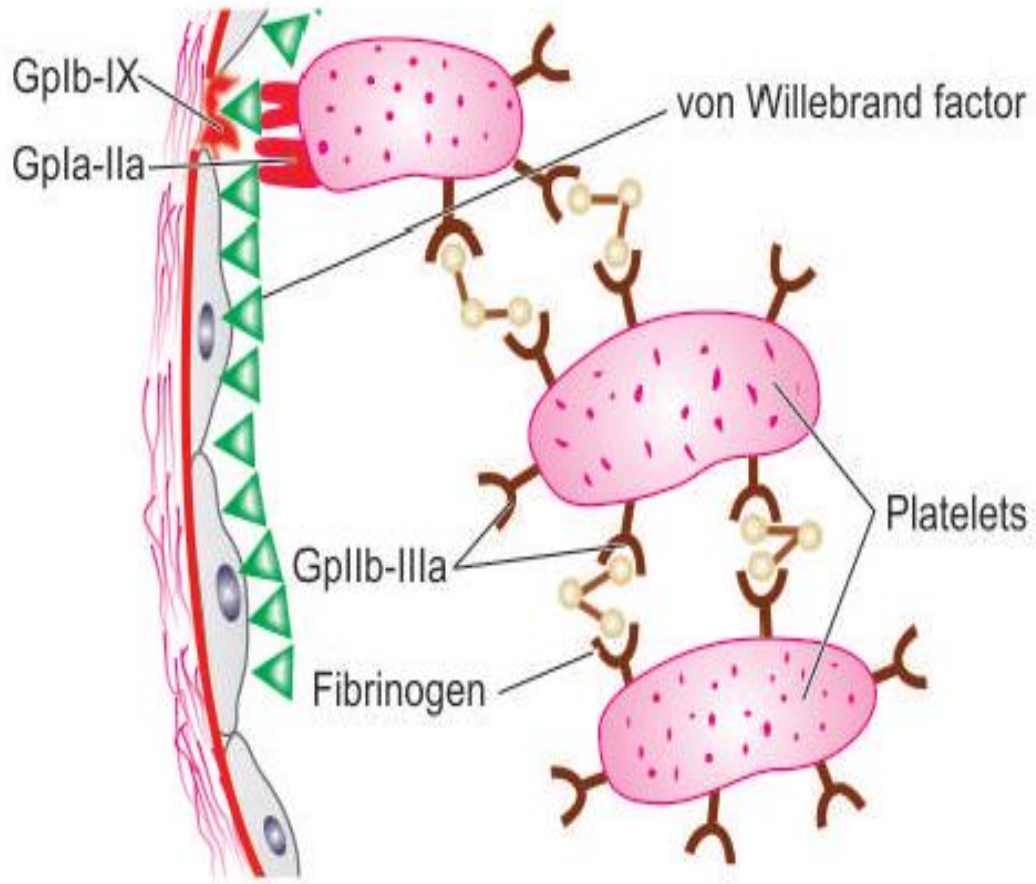
- Platelets adhere to collagen in the subendothelium due to presence of receptor on platelet surface, glycoprotein (Gp) Ia-IIa and Gp Ib-IX
- The adhesion to the vessel wall is further stabilised by von Willebrand factor, an adhesion glycoprotein.
- Vwf forms a bridge between collagen of endothelium and platelet



## 2) Platelet activation and Secretion

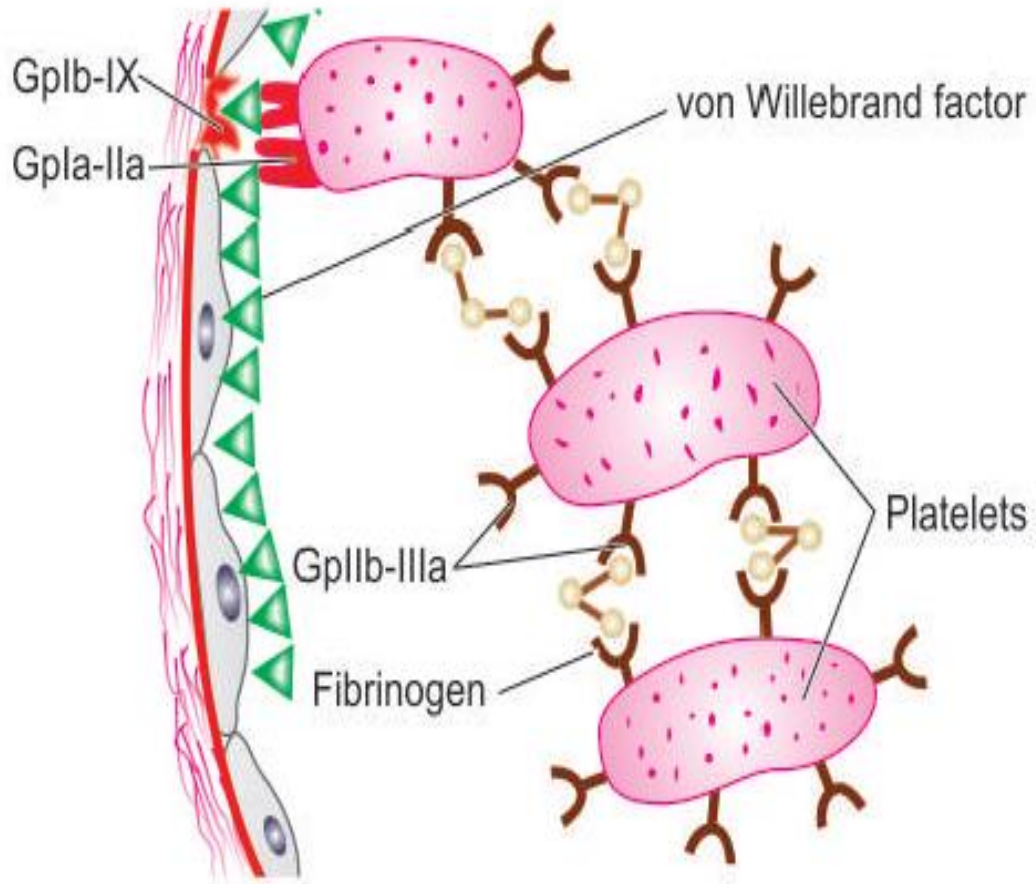
- After adhesion, platelets get activated and secrete their contents which are stored in two granules:-
  - **i) Alpha granules:** Contain fibrinogen, fibronectin, factor V & VIII, PDGF, TGF-B and platelet factor 4.
  - **ii) Dens bodies or delta-granules:** Contain *ADP, Ca, histamine, serotonin* and epinephrine.





### 3) Platelet aggregation

- Adherence of platelets to one another.
- Platelet membrane glycoprotein **IIb-IIIa** helps in aggregation.
- The most important endogenous stimulators of platelet aggregation are ADP and thromboxane A<sub>2</sub>
- It forms primary hemostatic plug which is reversible.
- After this coagulation system is activated forming a secondary (definitive) hemostatic plug which is irreversible



# Pathophysiology

- Virchow described three primary events which predispose to thrombus formation (**Virchow's triad**):

✓ Endothelial injury →

Activation of platelets

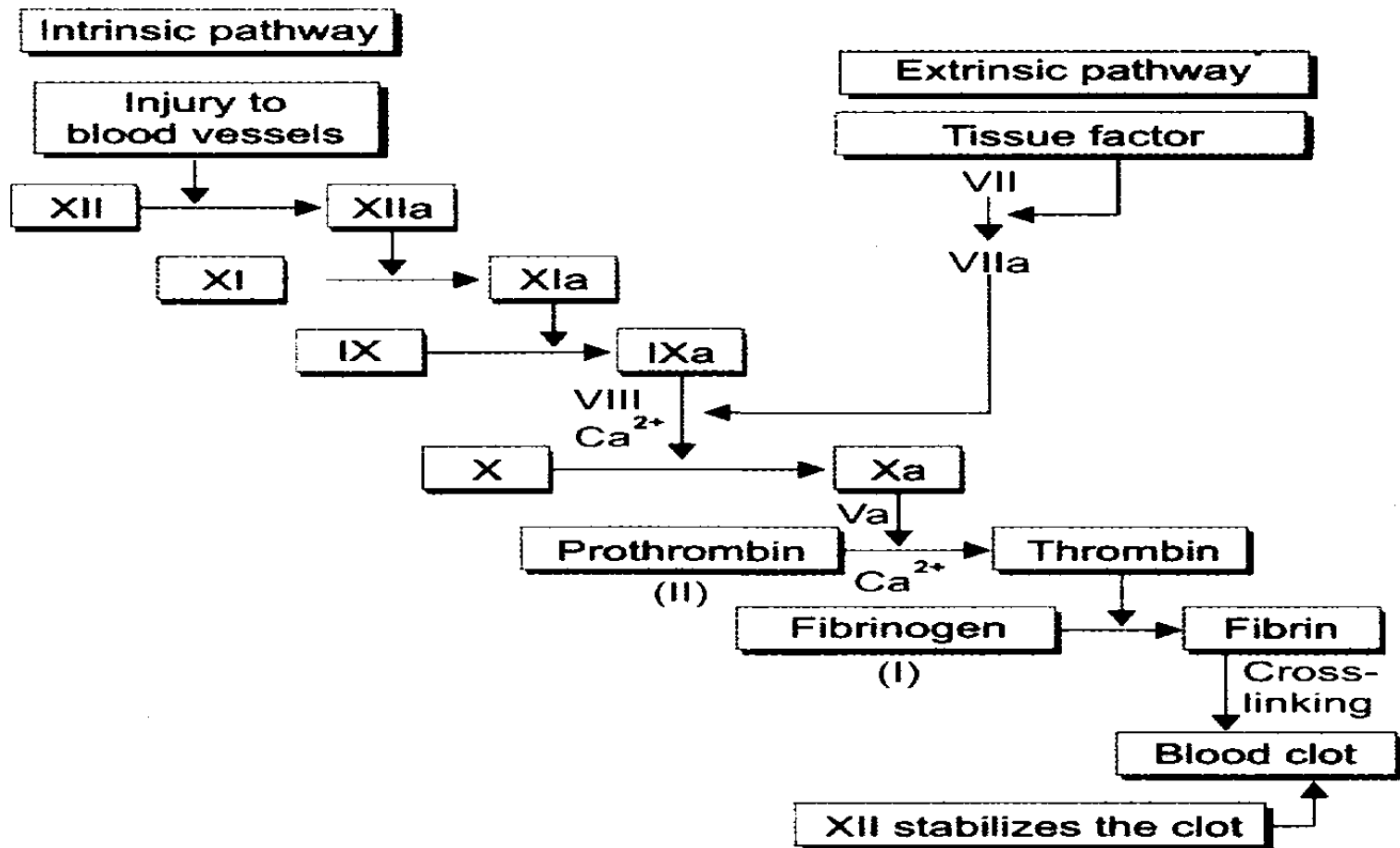
Activation of clotting system

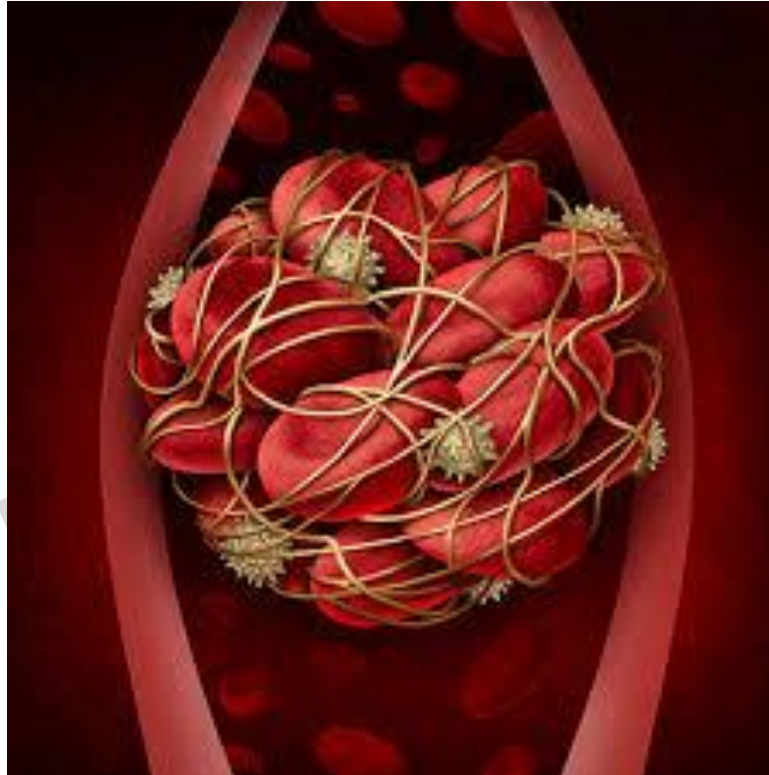
✓ Altered blood flow

✓ Hypercoagulability of blood.

# **ACTIVATION OF COAGULATION SYSTEM**

- Coagulation mechanism is the conversion of the plasma fibrinogen into solid mass of fibrin
- cascade of intrinsic (blood) pathway, the extrinsic (tissue) pathway, and the common pathway leading to formation of fibrin polymers.





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# Pathophysiology

- Virchow described three primary events which predispose to thrombus formation (**Virchow's triad**):

- ✓ Endothelial injury →

Activation of platelets

Activation of clotting system

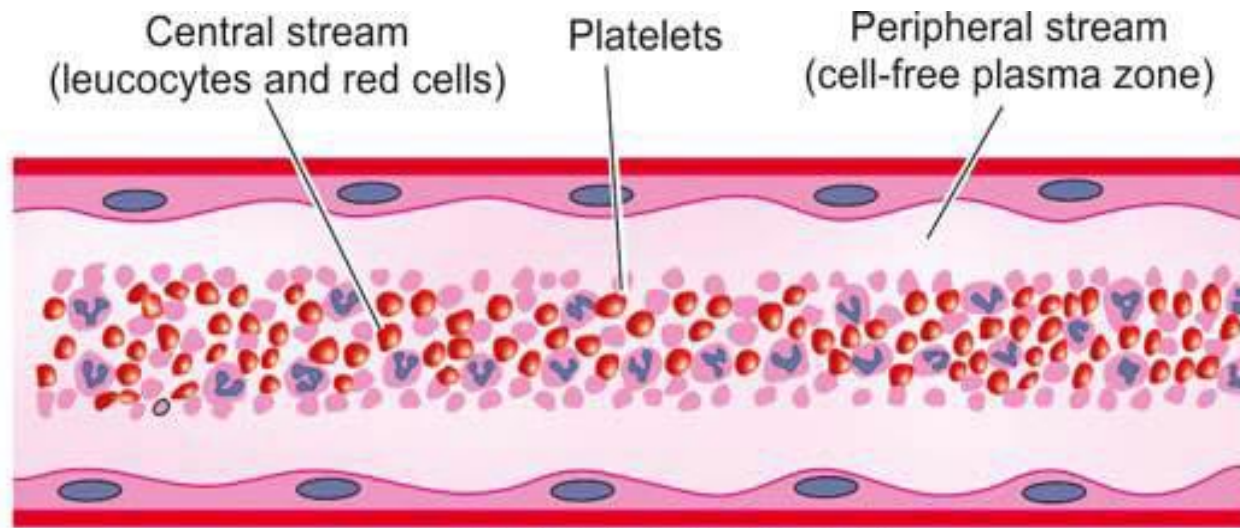
- ✓ Altered blood flow

- ✓ Hypercoagulability of blood.



## 2. ALTERATION OF BLOOD FLOW

- Normally, there is **axial/Laminar flow of blood**
  - The most rapidly-moving **central stream** consists of leucocytes and red cells.
  - The platelets are present in the slow-moving laminar stream **adjacent to the central stream**
  - The **peripheral stream** consists of most slow-moving cell-free plasma close to endothelial layer
- **ie. Platelets separated from endothelium by a slower moving layer of plasma**



A, NORMAL AXIAL FLOW

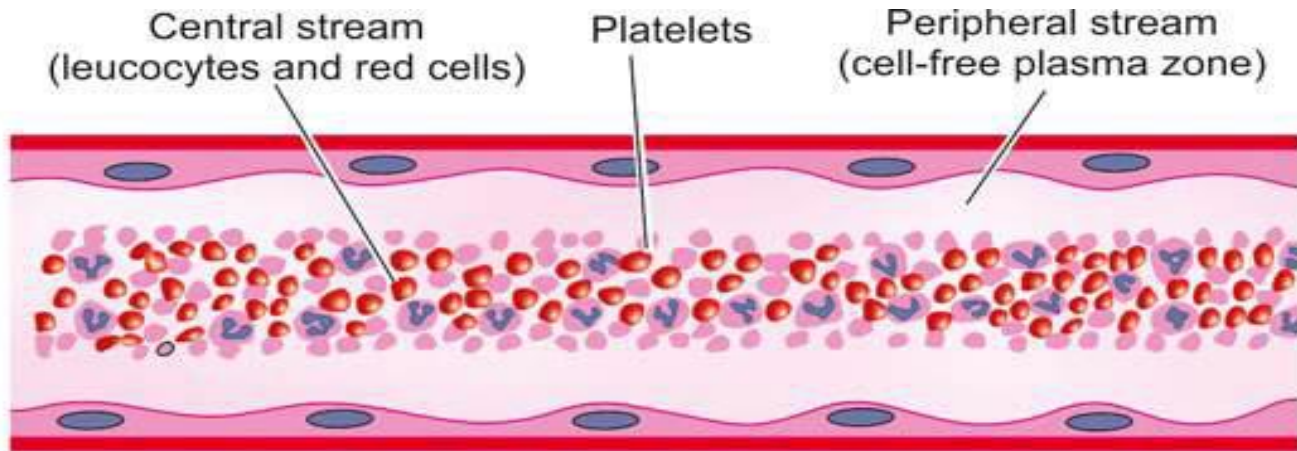
# ALTERATION OF BLOOD FLOW→

- **Turbulence** means unequal flow
- **Stasis** means slowing

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# Turbulence and stasis → normal axial flow of blood is disturbed → Thrombosis

- Endothelial injury → Promote endothelial activation, enhancing procoagulant activity
- Disrupt laminar flow and bring platelets into contact with the endothelium
- Prevent washout of activated clotting factors by fresh flowing blood
- Prevents inflow of clotting factor inhibitors



A, NORMAL AXIAL FLOW



B, MARGINATION AND PAVEMENTING

**Turbulence** → arterial and cardiac  
thrombi

**Stasis** → venous thrombi

# Pathophysiology

- Virchow described three primary events which predispose to thrombus formation (**Virchow's triad**):

- ✓ Endothelial injury →

Activation of platelets

Activation of clotting system

- ✓ Altered blood flow

- ✓ Hypercoagulability of blood.

### **3. HYPERCOAGULABLE STATES (THROMBOPHILIA)**

- **Hypercoagulability (also called thrombophilia) can be defined as any disorder of the blood that predisposes to thrombosis.**

**2 Types →**

- **Hereditary or primary**
- **acquired or secondary**



## INHERITED (PRIMARY) FACTORS

- i) Deficiency of antithrombin III
- ii) Deficiency of protein C
- iii) Deficiency of protein S
- iv) Mutation in factor V Leiden
- v) Defects in fibrinolysis (dysfibrinogenaemia, plasminogen disorders)
- vi) Increased levels of coagulations factors (II and VIII)

## ACQUIRED (SECONDARY) FACTORS

### a) *Risk factors:*

- i) Advancing age, ii) prolonged bed-rest, iii) prolonged immobilisation (e.g. in plaster cast, long distance travel), iv) cigarette smoking, v) obesity

### b) *Predisposing clinical conditions:*

- i) Heart diseases (e.g. myocardial infarction, CHF, rheumatic mitral stenosis, cardiomyopathy)
- ii) Vascular diseases (e.g. atherosclerosis, aneurysms of the aorta and other vessels, varicosities of leg veins)
- iii) Hypercoagulable conditions (e.g. polycythaemia, myeloproliferative disorders, dehydration, nephrotic syndrome, disseminated cancers)
- iv) Shock
- v) Tissue damage e.g. trauma, fractures, burns, major surgery on bones, abdomen or brain.
- vi) Late pregnancy and puerperium
- vii) Certain drugs (e.g. anaesthetic agents, oral contraceptives, hormonal replacement therapy).

### c) *Antiphospholipid antibody (APLA) syndrome:*

- i) Lupus anticoagulant antibody
- ii) Anti-cardiolipin antibody

## INHERITED (PRIMARY) FACTORS

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### c) *Antiphospholipid antibody (APLA) syndrome:*

- i) Lupus anticoagulant antibody
- ii) Anti-cardiolipin antibody

- Most common inherited cause of thrombosis is due to mutation in **factor V gene called Leiden mutation**
- This results in formation of defective (mutated) factor V called factor V Leiden which causes unchecked coagulation.

Cancers causing thrombosis are →

1. **Pancreas** (most common)
2. **Lung** (2nd most common)
3. Others → breast, stomach, prostate, pancreas, lymphomas, ovary and acute promyelocytic leukemia.

The coexistence of peripheral venous thrombosis with visceral malignancy is called **Trousseau's syndrome (migratory thrombophlebitis)**.

## Conditions with both arterial and venous thrombi

<ul style="list-style-type: none"><li>• Homocysteinuria<sup>a</sup></li><li>• Antiphospholipid antibody<sup>a</sup></li><li>• Hyperhomocysteinemia<sup>a</sup></li><li>• Disseminated intravascular coagulation<sup>a</sup></li><li>• Heparin induced thrombocytopenia<sup>a</sup></li></ul>	<ul style="list-style-type: none"><li>• Essential thrombocythemia<sup>a</sup></li><li>• Cancer<sup>a</sup></li><li>• PNH<sup>a</sup></li><li>• Polycythemia vera<sup>a</sup></li><li>• Dysfibrinogenemia<sup>a</sup></li></ul>
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# Pathophysiology

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- ✓ Altered blood flow
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# OVERVIEW

- Definition
- Pathogenesis
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- Fate of thrombus



# **Types of Thrombi**

3 Types depending on site of origin→

**1. Cardiac thrombi**

**2. Arterial thrombi**

**3. Venous thrombi**

- **Venous thrombi** are called as **stasis thrombi** because they are formed in the sluggish venous circulation. These are also known as **red thrombi** as they contain more enmeshed red cells and relatively few platelets.

- **Arterial thrombus** contains **more platelets** and relatively less fibrin

- **Thrombi on heart valves** are called **vegetations**

# OVERVIEW

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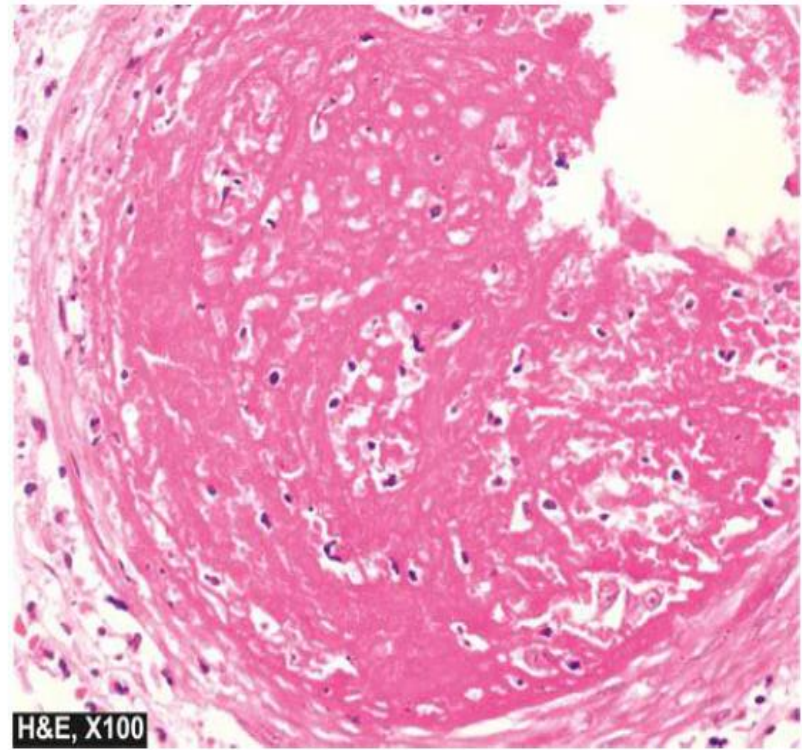
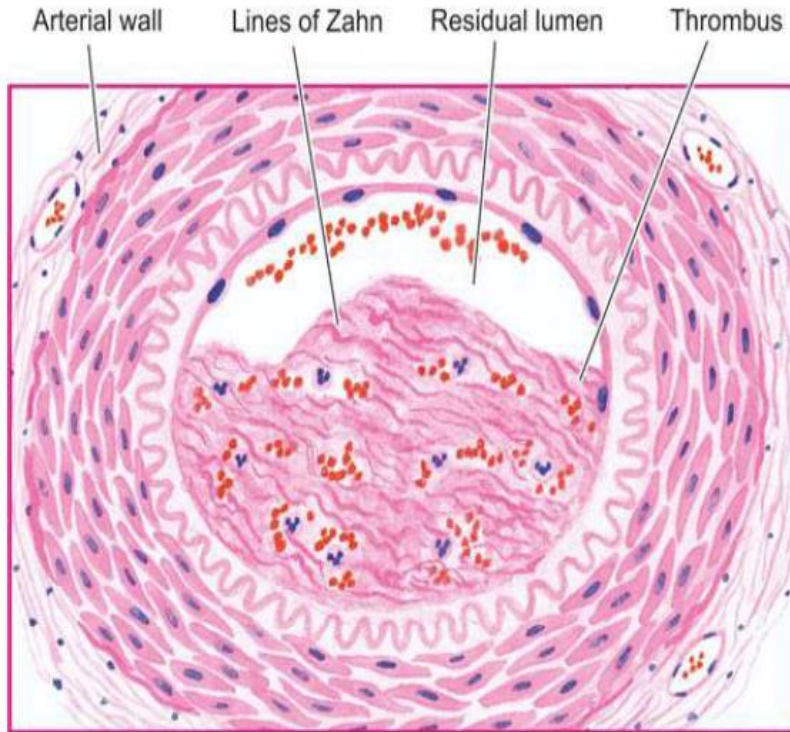
# **Grossly**

Thrombi may be of various shapes, sizes and composition depending upon the site of origin.

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# Arterial thrombi

- tend to be **white and mural** → firm and pale.
- **Lines of Zahn present** → alternate layers of light-staining aggregated platelets admixed with fibrin meshwork and dark-staining layer of red cells
- Thrombus with lines of Zahn is also called **coralline thrombus**

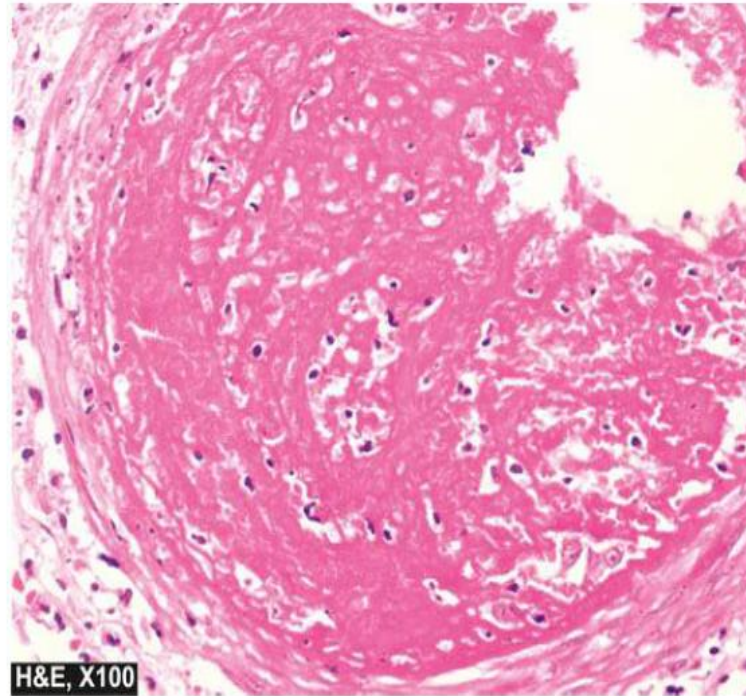
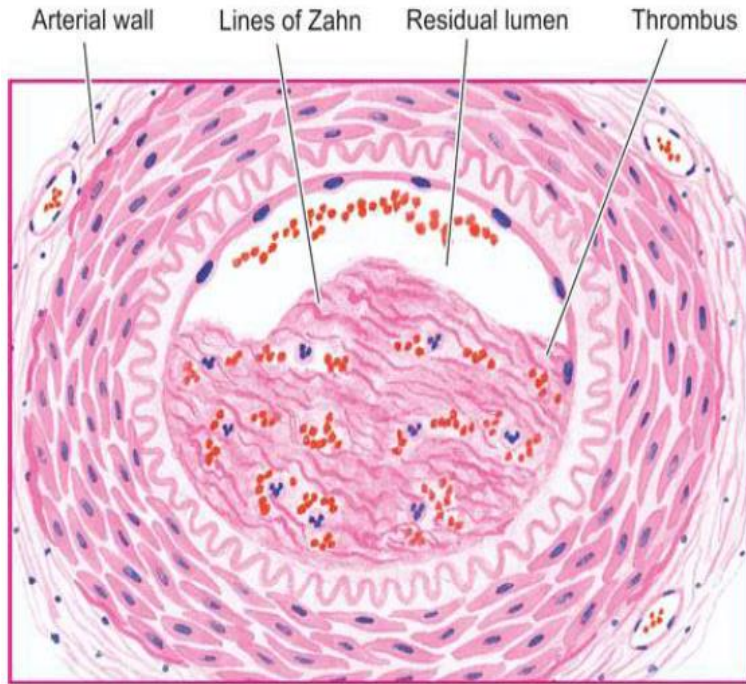


**Figure 4.24** Thrombus in an artery. The thrombus is adherent to the arterial wall and is seen occluding most of the lumen. It shows lines of Zahn composed of granular-looking platelets and fibrin meshwork with entangled red cells and leucocytes.

# Venous thrombi

- Red and occlusive → soft, red and gelatinous
- Lines of Zahn absent





**Figure 4.24** Thrombus in an artery. The thrombus is adherent to the arterial wall and is seen occluding most of the lumen. It shows lines of Zahn composed of granular-looking platelets and fibrin meshwork with entangled red cells and leucocytes.



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# Clinical Effects

- **1. Cardiac thrombi** Large thrombi in the heart may cause sudden death by mechanical obstruction of blood flow or through thromboembolism to vital organs.

- **2. Arterial thrombi** These cause ischaemic necrosis of the deprived part (infarct) which may lead to gangrene.

### 3. Venous thrombi (Phlebothrombosis)

- i) Thromboembolism
- ii) Oedema of area drained
- iii) Poor wound healing
- iv) Skin ulcer
- v) Painful thrombosed veins (thrombophlebitis)
- vi) Painful white leg (phlegmasia alba dolens) due to ileofemoral venous thrombosis in postpartum cases
- vii) Thrombophlebitis migrans in cancer.

# OVERVIEW

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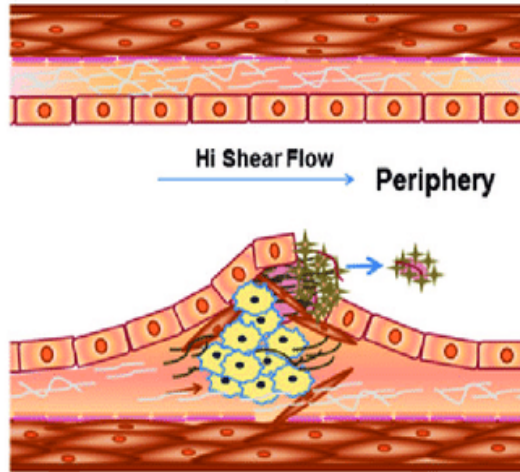
Feature	Arterial thrombus	Venous thrombus
Pathogenesis	Endothelial injury or site of turbulence	Stasis of blood
Blood flow	Associated with <b>active</b> blood flow	Associated with sluggish blood flow
Sites	Coronary, cerebral and femoral arteries	Superficial and deep leg veins, ovarian/periuterine veins
Propagation	Grows in a <b>retrograde manner</b> from point of attachment	Grows in an antegrade manner from point of attachment
Gross	Lines of Zahn <b>present</b>	Lines of Zahn absent
Microscopic	Pale platelet layer alternating with dark red cell layer so also called as <b>white thrombi</b>	Red cells mixed with relatively less platelets, so also called as red thrombi
Occlusion	<b>Incomplete</b> lumen occlusion	Complete vessel occlusion
Complications	Ischemia and infarction of organs	Embolism, edema and ulceration

FEATURE	ARTERIAL THROMBI	VENOUS THROMBI
1. <i>Blood flow</i>	Formed in rapidly-flowing blood of arteries and heart	Formed in slow-moving blood in veins
2. <i>Sites</i>	Common in aorta, coronary, cerebral, iliac, femoral, renal and mesenteric arteries	Common in superficial varicose veins, deep leg veins, popliteal, femoral and iliac veins
3. <i>Thrombogenesis</i>	Formed following endothelial cell injury e.g. in atherosclerosis	Formed following venous stasis e.g. in abdominal operations, child-birth
4. <i>Development</i>	Usually mural, not occluding the lumen completely, may propagate	Usually occlusive, take the cast of the vessel in which formed, may propagate in both directions
5. <i>Macroscopy</i>	Grey-white, friable with lines of Zahn on surface	Red-blue with fibrin strands and lines of Zahn
6. <i>Microscopy</i>	Distinct lines of Zahn composed of platelets, fibrin with entangled red and white blood cells	Lines of Zahn with more abundant red cells
7. <i>Effects</i>	Ischaemia leading to infarcts e.g. in the heart, brain etc	Thromboembolism, oedema, skin ulcers, poor wound healing

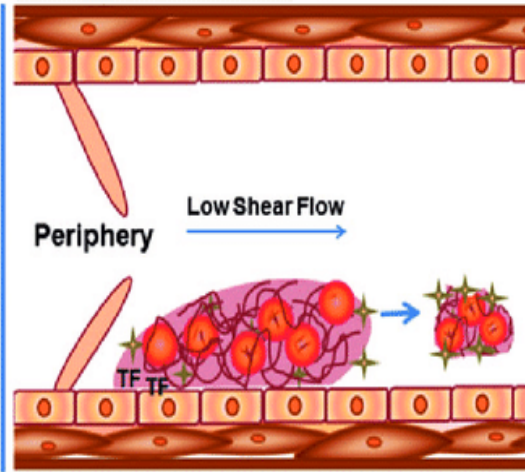
Feature	Arterial thrombi	Venous thrombi
• Blood flow	• Formed in rapidly-flowing blood of arteries & heart	• Formed in slow moving blood in veins.
• Sites	• Coronary (most common), cerebral & femoral arteries	• Superficial veins of lower limb, deep veins of lower limb → femoral, popliteal & iliac.
• Thrombogenesis	• Due to endothelial injury by turbulence	• Due to stasis
• Development	• Usually mural not occluding the lumen completely	• Almost invariably occlusive
• Propagation	• In retrograde direction	• In antegrade direction towards the heart.
• Macroscopy	• Grey white	• <b>Red-Blue</b>
• Microscopy	• Distinct lines of Zahn composed of platelets, fibrin, RBC & WBC	• Lines of Zahn are not so distinct (mainly RBCs)
• Effects	• Ischemia leading to infarcts e.g., of brain, heart	• Edema, ulcer, poor wound healing
• Emboli	• Less common	• More common



**A Arterial Thrombosis**



**B Venous Thrombosis**





Mural  
thrombus



Occlusive  
thrombus



Embolus

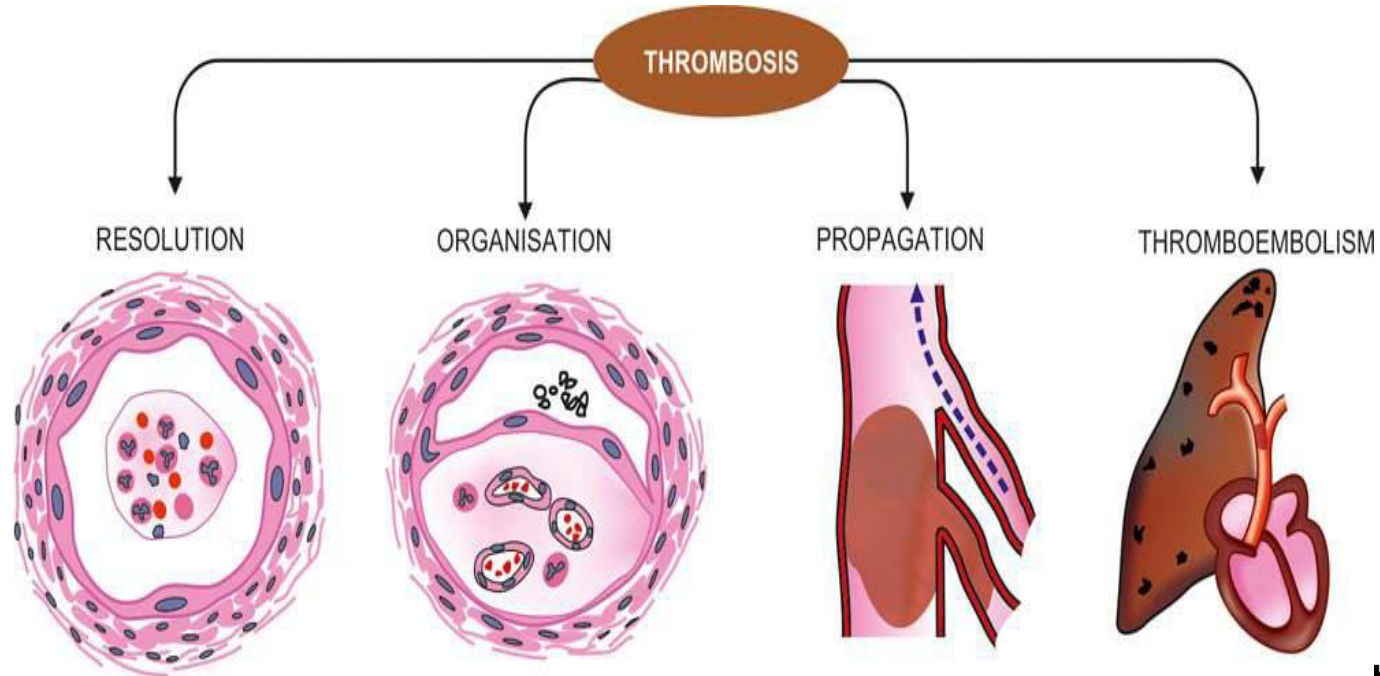
# Red thrombi (antemortem) have to be distinguished from postmortem clots

FEATURE	ANTEMORTEM THROMBI	POSTMORTEM CLOTS
1. <i>Gross</i>	Dry, granular, firm and friable	Gelatinous, soft and rubbery
2. <i>Relation to vessel wall</i>	Adherent to the vessel wall	Weakly attached to the vessel wall
3. <i>Shape</i>	May or may not fit their vascular contours	Take the shape of vessel or its bifurcation
4. <i>Microscopy</i>	The surface contains apparent lines of Zahn	The surface is 'chicken fat' yellow covering the underlying red 'currant jelly'

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- Gross
- Clinical features
- Differences between arterial and venous thrombosis
- Fate of thrombus

# Fate of Thrombus



# OVERVIEW

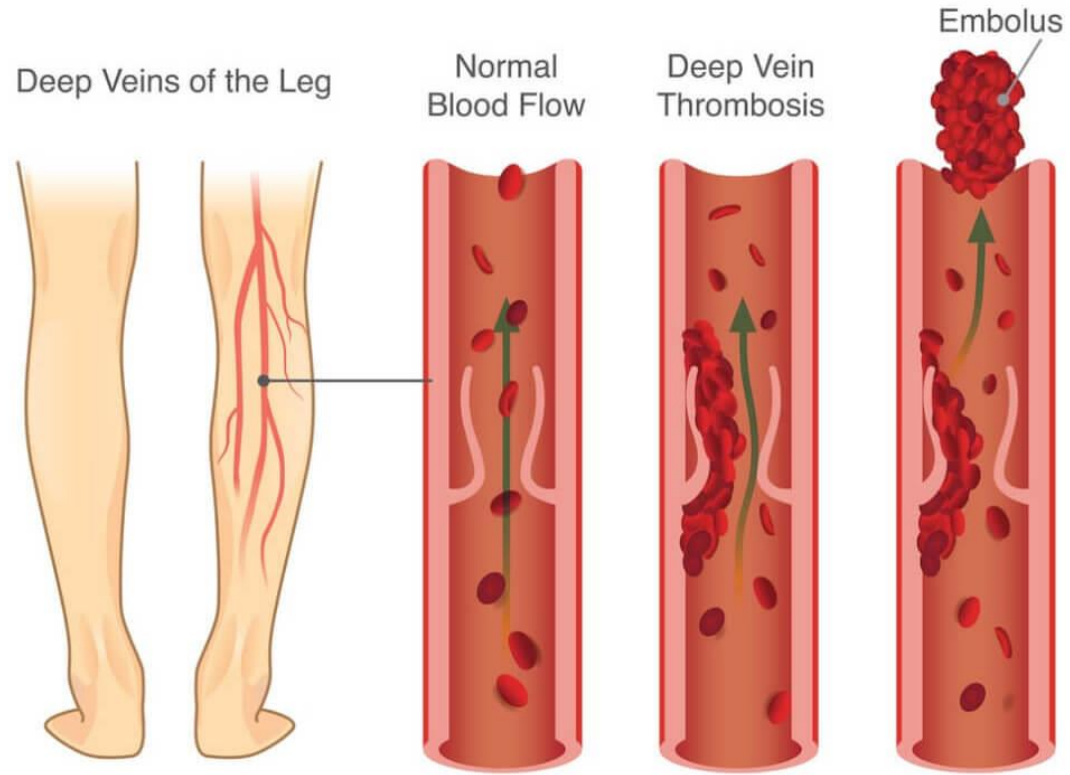
- Definition
- Pathogenesis
- Types
- Gross
- Clinical features
- Differences between arterial and venous thrombosis
- Fate of thrombus

- **Oedema**
- **Hyperamia and congestion**
- **Thrombosis**
- **Embolism**
- **Ischemia**
- **Infaction**
- **Shock**

# EMBOLISM

- An embolus is a detached intravascular solid, liquid, or gaseous mass that is carried by the blood from its point of origin to a distant site, where it often causes tissue dysfunction or infarction.
- The transported intravascular mass detached from its site of origin is called an **embolus**





# THANK YOU

Dr. PRIYANKA SACHDEV

*follow us*



**Dr. PRIYANKA SACHDEV**

**Thank you for being awake**



**Dr. PRIYANKA SACHDEV**

# FEEDBACK PLEASE



med[LIVE]

# NEXT CLASS

- Every **MWF** (Monday , Wednesday , Friday) → **PATHOLOGY**
- Every **TTS** (Tuesday , Thursday , Saturday) → **PHARMACOLOGY**

FREE LIVE CLASSES

COMPLETE

# PHARMACOLOGY

By Dr Priyanka Sachdev

10 Nov - Pharmacokinetics part 1  
17 Nov - Pharmacokinetics part 2  
19 Nov - Pharmacodynamics  
21 Nov - ANS part 1  
24 Nov - ANS part 2  
26 Nov - ANS part 3  
28 Nov - Drugs for Asthma  
01 Dec - Oral Hypoglycaemic Agents and Insulin  
03 Dec - CNS - Sedatives and hypnotics, Alcohol  
05 Dec - CNS - Anti Parkinson's drug  
08 Dec - Drugs affecting RAS  
10 Dec - Anti-angina and Heart failure drugs  
12 Dec - Diuretics, Antidiuretics  
15 Dec - Antimicrobials part 1  
17 Dec - Antimicrobials part 2

EVERY TTS  
4 - 6 PM



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# PATHOLOGY

By Dr Priyanka Sachdev

11 Nov - Cell Adaptation and injury  
16 Nov - Inflammation  
18 Nov - Hemodynamics  
20 Nov - Neoplasia part 1  
23 Nov - Neoplasia part 2  
25 Nov - Disorders of RBC 1  
27 Nov - Disorders of RBC 2  
02 Dec - Disorders of WBC  
04 Dec - Disorders of platelets  
07 Dec - Cardiovascular system  
09 Dec - Respiratory system  
11 Dec - GIT / Liver  
14 Dec - Renal system  
16 Dec - Practical and Viva voce (2nd Prof)

EVERY MWF  
4 - 6 PM

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# TOMORROW

- 21<sup>th</sup> Nov → SATURDAY →  
PHARMACOLOGY → ANS
- 23<sup>th</sup> Nov → MONDAY → PATHOLOGY →  
NEOPLASIA

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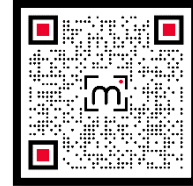




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